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GENERAL PRACTICE CLINICS

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INTERNATIONAL RECORD OF MEDICINE

ATYPICAL FORMS OF PATHOGENIC MYCOBACTERIA — *Eleanor Alexander-Jackson*

CLINICAL STUDIES ON ANTICANCER AGENTS, 1952-53 — *John R. Sampey*

PSYCHOPATHOLOGY FOR THE GENERAL PRACTITIONER

THE REPRODUCTION OF PSYCHOSIS IN SCIENCE FICTION — *Robert Plank*

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ADVANCE REPORTS AND HIGHLIGHTS FROM CURRENT MEDICAL MEETINGS

Featured in this issue are abstracts of a group of papers on Geriatrics that were presented at the Annual Meeting of the National Vitamin Foundation and the Johns Hopkins University School of Hygiene and Public Health.

Also included are abstracts of papers delivered before the American Association of Pathologists and Bacteriologists; Philadelphia County Medical Society, Postgraduate Institute and Convention; Philadelphia County Medical Society, Scientific Meeting; Chicago Medical Society; Dallas Southern Clinical Society; Medical Research Forum, New York Academy of Medicine; Nutrition Institute of the Federation of American Societies for Experimental Biology.

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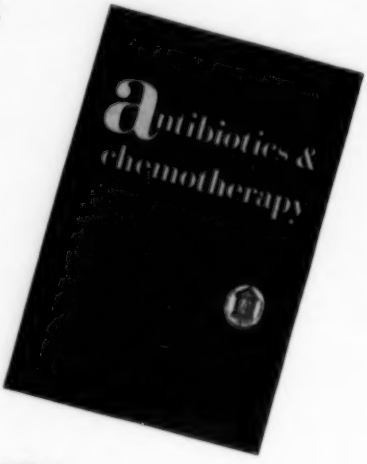

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How **MULL-SOY** *feeding from birth dispels the shadow of major allergy*

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POTENTIALLY ALLERGIC CHILDREN (offspring or siblings of one or more persons with one or more allergic diseases)	NO. OF CHILDREN	INCIDENCE OF MAJOR ALLERGY TO 6 YEARS
CONTROL GROUP #1* (siblings of experimental group)	65	64.6%
CONTROL GROUP #2* nonrelated; (carefully selected from 4,710 children in 1,215 allergic families for similar parental and sibling allergic backgrounds)	175	52.0%
EXPERIMENTAL GROUP (Cow's milk withheld from birth; 3 breast fed, 5 on meat base formulas, 88 on MULL-SOY; cow's milk introduced later)	96	14.6%

% 10 20 30 40 50 60 70 80 90 100

*Observed for same lengths of time as counterparts in experimental group. Table adapted from: Glaser, J., and Johnstone, D. E.: Prophylaxis of Allergic Disease in the Newborn, J. A. M. A. 153:620, Oct. 17, 1953.

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Atypical Forms of Pathogenic Mycobacteria

*Eleanor Alexander-Jackson, Ph.D.**

NEWARK, N. J.

During the last 25 years, atypical forms of bacteria have usually been regarded as unworthy of serious consideration. The reports of earlier pioneers concerning reproductive granules and filterable forms were discounted as misinterpretations following faulty methods of experimentation. Superior modern working tools such as the micromanipulator, for isolating single organisms in microdroplets; the electron microscope and the phase microscope, for revealing details of structure; the television microscope; improved photomicrography; and moving pictures have all made it possible to demonstrate in more convincing ways that variations in morphology are not necessarily abnormal and that atypical forms are often of great significance.

Variations in morphology and reproduction appear to arise as a response to environmental conditions experienced by microorganisms in various hosts or culture media. In general, an environment favorable to vigorous growth of an organism results in forms that differ markedly from those of the same organisms grown under unfavorable conditions. Both in the animal body and in the test tube these conditions may include one or more of the following unfavorable factors:

1. Insufficient amounts or varieties of needed metabolites or trace substances, such as certain metallic ions or vitamins.
2. Too high or too low a concentration of hydrogen ions or oxygen tension.
3. Antimetabolites, which "fool" the organism by replacing necessary food substances with related but unneeded chemicals, such as the nicotinic hydrazides in tuberculosis therapy.
4. Antibiotics, which inhibit growth or kill.
5. Antibodies given passively by administration of antisera or developed by the infected host, which agglutinate and lyse the infecting organisms.

Let us now consider variations in the family of Mycobacteria, which lie between the true bacteria and the fungi. By virtue of certain lipopolysaccharides that con-

*Dr. Alexander-Jackson is with the Cancer Research Laboratories, Newark, New Jersey.

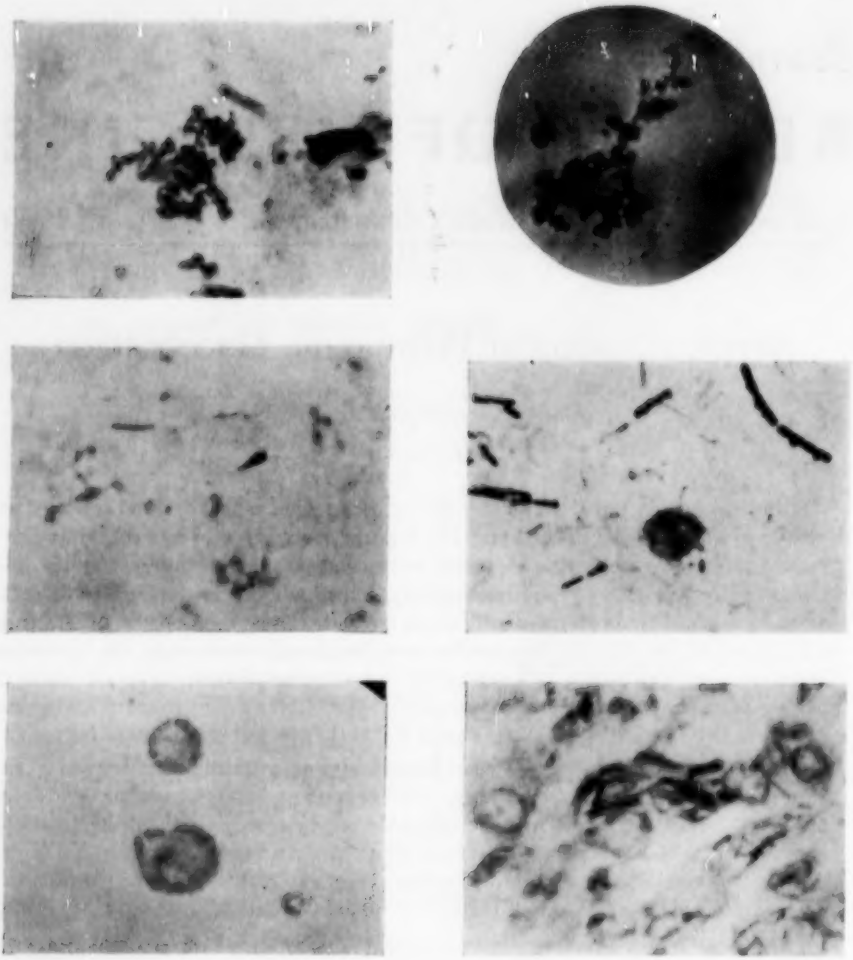


FIG. 1. (top, left) Zoogleal forms from tuberculous pleural fluid, Alexander-Jackson's Triple Stain, X 1200.

FIG. 2. (middle, left) Developing globoid body in rod from blood culture, aged six months, Hansen's disease, X 1328.

FIG. 3. (bottom, left) Large globoidal ring forms breaking up into rods, from Hansen's disease blood culture, Alexander-Jackson's Triple Stain, X 2500.

FIG. 4. (top, right) Fungoidal zoogleal form with developing ring forms, non-acid-fast, from Hansen's disease blood culture, X 1200.

FIG. 5. (middle, right) Acid-fast globus with protruding rod, acid-fast rods in a motile six month old culture from Hansen's disease blood culture, X 1328.

FIG. 6. (bottom, right) Intracellular acid-fast rods, splenic abscess of mouse inoculated with blood culture obtained from patient with Wilson's disease, X 1328.

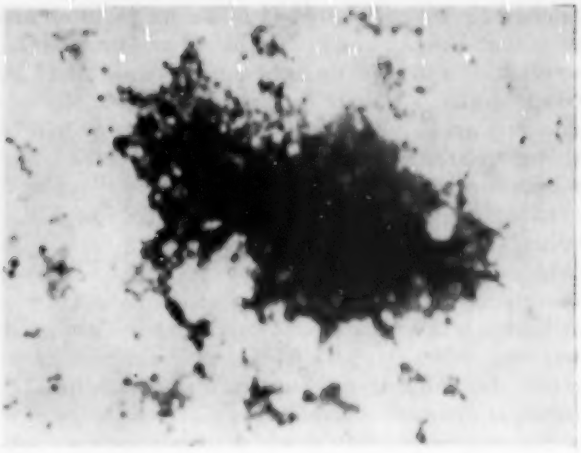


FIG. 7. Large zoogleal symplasm from blood culture of patient with Hansen's disease, Ziehl-Neelsen, Victoria blue, X 2500.

tain mycolic acid, these bacteria hold fast to phenolized basic fuchsin dye in the presence of acids or acidified alcohol. They are thus fast to acid or to acid-alcohol. The only other organisms that possess this unique chemical property are the Proactinomycetes (Nocardia), which are so closely related to the Mycobacteria that certain species are difficult to place in one group or the other.[1,12] The Mycobacteria are more fungoidal in their developmental pattern than the true bacteria. Rudimentary mycelia with branching are not uncommon and have been demonstrated in the electron microscopic photographs of Brieger and Glauert,[2] in their study of avian strains of *Mycobacterium tuberculosis*. Koch interpreted certain bodies as spores,[3] stating: "Under certain conditions, to be mentioned later, the bacilli form spores even in the animal body; and indeed, the single bacillus contains several, usually 2 to 4 spores of oval form which are distributed throughout its length."

I shall discuss in the following paragraphs various forms of the Mycobacteria that I have observed and studied in detail: *M. tuberculosis*[4] (1945); *Mycobacterium leprae* (human), first grown in transferable culture by me (1951);[5] *Sclerobacillus Wuerthele-Caspé* (1947); a mycobacterium-like organism consistently isolated by Dr. Virginia Wuerthele-Caspé and myself from human and animal cancer (1948 to 1953);[6, 7, 8] and a previously unknown mycobacterium-like organism from two patients with Wilson's disease (hepatolenticular degeneration).[9] The forms to be described include (1) filterable virus-like forms, (2) zoogleal symplasms or matrix forms, (3) ring forms, globoid bodies, and cysts, and (4) rods and filaments.

FILTERABLE FORMS

Electron microscopic studies of pure cultures of these mycobacteria have revealed submicroscopic bodies ranging in size from 20 to 70 mμ. These minute forms, of virus dimensions, pass through cellulose filter pads (Seitz) or fritted glass. After a

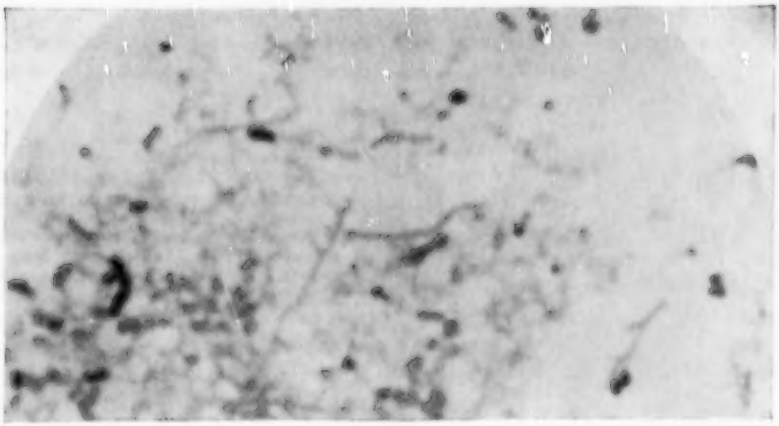
prolonged period of incubation in the special broth developed in our laboratory,[8] or passage through chick embryos, larger forms developed in the filtrates, which were readily seen under the light microscope and which grew out into visible colonies on egg slants. The Rous chicken sarcoma agent, studied in this way, has developed into motile rods. When the rods were removed by Seitz filtration, the filtrates slowly redeveloped rod forms. This result would appear to preclude the interpretation that a contaminating bacillus was carrying a virus "on its back," though such a phenomenon has been shown to exist in cultures of bacilli infected by viruses (bacteriophages).

In the course of my study of pure cultures of *M. tuberculosis* with the Chambers micromanipulator, I found a microdroplet which appeared at first to be optically clear, but which after several days developed some active granules. This droplet was then sucked up by the micropipet and expelled into a small amount of broth in a test tube. After several months, the granules had developed into a culture consisting of a mixture of granules and short rods, many of which were acid-fast. These organisms grew out very slowly as colonies on egg slants, and when inoculated into a guinea pig caused enlarged inguinal glands and a positive tuberculin reaction. It would seem that the granular culture contained viable forms of the tubercle organism which had grown out from submicroscopic bodies present in the microdroplet.

A mycobacterium-like organism was isolated and cultivated by me from the blood of 25 leprosy patients. Cultures of this organism, inoculated into white mice, were "vertically transmitted" through two more uninoculated generations. The young of the third generation were actually spotted with ulcerative lesions containing nests of acid-fast organisms even *in utero*, as was shown by sacrificing one of the pregnant mice of the second generation which had already given birth to two previous litters similarly ulcerated. The organisms were also recovered in cultures made from the spotted baby mice and from the maternal placenta, thus fulfilling Koch's postulates. Infection via the placenta indicates that the infectious agent was initially very minute.

MATRIX FORMS (ZOOGLEAL OR SYMPLASM FORMS)

These plasmodial forms, consisting of granules of various sizes embedded or enmeshed in amorphous material, were observed by me in tuberculous fluids and in broth cultures of the tubercle bacillus when stained by my triple-stain[10] modification of the Ziehl-Neelsen technic. They were often present in large numbers in pleural or spinal fluids from tuberculosis patients in whom acid-fast rods had not been found. Some of these specimens came from streptomycin-treated patients who several months later showed acid-fast bacilli. Ten years of study of *unstained* matrix or plasmodial zoogleal forms in microdroplets made from pure cultures of well-known strains of *M. tuberculosis* convinced me that the granule bodies in these amorphous masses were capable of becoming orthodox rods. A few years later, I repeatedly observed this same developmental process taking place in a large number of hanging drops made from blood cultures of the organism I had cultured from the blood of leprosy patients. Moving pictures and photomicrographs confirmed my observations.



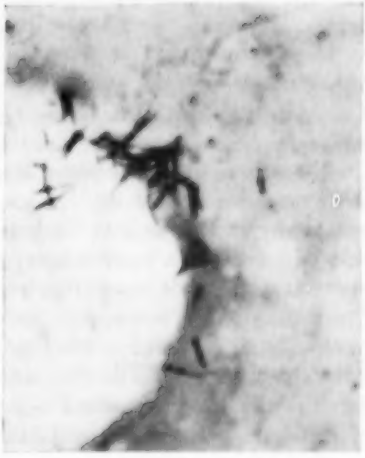


FIG. 8. (top) Various forms of the mycobacterium-like organism grown from the blood and tumors of humans and animals suffering from cancer, isolated from a mouse tumor, and showing mycelial filaments, rods, coccobacilli, and coccoidal granules, Ziehl-Neelsen stain, X 2500.
FIG. 9. (bottom, left) Culture made from the organs of a leukotic chicken and allowed to age several months; note ring forms, one with protruding rod.
FIG. 10. (bottom, right) Pointed needle-like rods observed on a direct smear of blood obtained from a child with leukemia, Alexander-Jackson's Triple Stain, X 1328.

The matrix forms are found especially in body fluids and in primary blood cultures. In pure cultures of acid-fast rods, incubated in the presence of normal rabbit serum or antibiotics, the bacilli swelled up, showed increased granulation, and after three weeks had become amorphous zoogleal masses. In the presence of immune rabbit serum, further changes into globoid bodies, which will be mentioned later, took place. The effect of normal serum suggested that the bacterial outer membranes were lysed by some enzyme or antibody, like alexin, normally present in blood.

FIG. 11. Motile rods cultured from the blood of a child suffering from a brain tumor (glioblastoma), Ziehl-Neelsen stain, showing development of small acid-fast granules within several of the rods. At autopsy, the brain also showed many acid-fast bodies, including ring forms similar to those in FIG. 7. X 1500.

Pericardial fluid of a young girl with tuberculosis, being treated with streptomycin, appeared to be bacillus-negative by the Ziehl-Neelsen staining method. However, the triple stain revealed large numbers of semi-acid-fast zoogleal masses. This fluid, cultured on Petragnani egg slants, grew out into acid-fast rods, which produced generalized tuberculosis in the guinea pig.

A woman suspected of having tuberculosis received negative sputum and x-ray reports. At the request of her physician, I examined a specimen of her sputum with the triple-stain technic. A number of suspicious semi-acid-fast granule and zoogleal forms were seen. I requested that another specimen be sent to me in a few weeks. The second specimen showed frank acid-fast rods. At this time, the patient also developed fever, and a positive x-ray finding was obtained. She was treated with streptomycin and made an excellent recovery.

The finding of atypical forms alone should not be considered to be diagnostic of disease, but rather to be a suspicious warning signal. Thus the patient whose sputum shows such forms should continue to be watched for at least another month rather than be dismissed with a negative report. If acid-fast rods develop within this period, treatment given promptly can halt the disease before it does great damage.

RING FORMS, GLOBOID BODIES, AND CYSTS

These globoid forms appear to arise under conditions unfavorable to normal growth and development, since they are found especially in treated or resistant patients and animals, and in cultures containing antibiotics, drugs or immune serum, or in old cultures. Ring forms can arise from a curling up of rods into closed circles. The larger and thinner walled cysts may develop from rings or enlargement of smaller globoidal granule bodies, or they may start by a swelling within the rod, resulting initially in a globoid "large body," which enlarges still further into a round or pear-shaped envelope, within which are seen granules, some of which may be acid-fast. The hypothesis is advanced that ring forms and cysts conserve the chromatin material of the microorganism under unfavorable environmental conditions. Too early discontinuance of treatment, or decrease in the resistance of persons with

arrested disease, results in proliferation of granules which later lengthen out into rods. In leprosy, the cyst walls often hold together as the sac enlarges, thus forming the globi of acid-fast rods so characteristic of Hansen's disease.

RODS AND FILAMENTS

The acid-fast rods of *M. tuberculosis* and *M. leprae* are familiar to all physicians and laboratory technologists. The early rod forms of the cancer organism are slender and needle-like, often with pointed ends. "Auer bodies" observed in certain types of cells in leukemia resemble rods of this type. Smears of malignant tissue stained by my triple stain often reveal very delicate acid-fast rods and filaments, some of which lie within the cytoplasm and even within the nucleus of tumor cells. Sclerodermal lesions revealed similar forms. Our pioneer work with "Sclerobacillus Wuerthele-Caspé" has been confirmed by Doctors N. Delmotte and L. Van der Meiren of the Pasteur Institute in Brussels.[11]

Blood cultures made from patients suffering from certain other diseases of obscure etiology have also yielded mycobacteriumlike organisms. These diseases include Boeck's sarcoid, lupus erythematosus, rheumatic arthritis, and Wilson's disease (hepatolenticular degeneration). The organism of the last named was grown from the blood of two patients with Wilson's disease and is described in detail elsewhere. Both cultures, when inoculated into mice and guinea pigs, produced a slowly developing parasitism characterized by intracellular acid-fast rods, fungoidal non-acid-fast matrix and rudimentary mycelial forms, accompanied by cell degeneration. Foam cells were found in the brain of one mouse, and cross-agglutination of Wilson's organisms in serum from a leprosy patient was noted. Whether the abnormal copper metabolism in patients with Wilson's disease is due to this newly found mycobacterium, or whether a genetic deficiency in the patient makes him susceptible to organisms of this type, is not yet known. Possibly such patients possess some genetic defect, but it is of interest that the mycobacteria isolated from both patients were pathogenic in a similar way for the inoculated animals and, moreover, produced lesions comparable with those found at autopsy in the human.

MOTILITY

Most textbooks state that mycobacteria are nonmotile. Calmette, however, has described rods in very young cultures of tubercle bacilli ("motile by virtue of flagella"). Jensen, in a "Symposium on the Actinomycetales"[12] (which include the mycobacteria and closely related coryneform bacteria), described motile forms of the Nocardia and corynebacteria. He concludes that "an alteration in the definition of the order Actinomycetales as constantly non-motile will therefore be necessary."

I described,[13] for the first time freely growing motile cultures of Hansen's bacillus, which I had grown from the blood of leprosy patients. Occasional motile forms in cultures of Hansen's bacillus had been noted by Vaudremer.[14]

Motile rod forms of the cancer isolate have been described by von Brehmer,[15] Glover and Clark,[16] Wuerthele-Caspé, and myself. Motile forms may be obtained

directly from tumor tissue or aspirated tumor fluid from patients with advanced cancer. Motile forms can be induced from nonmotile cultures grown in culture media containing such peptones as trypticase and phytone, or chick embryo.[8] An autoclaved chick-embryo agar devised by Wuerthele-Caspé is useful for inducing and maintaining motility. In old cultures, motile rods lengthen out into long filaments, which lose their motility and break up into sporelike bodies.

Motile rods were found to be highly virulent; doses of 0.2 to 0.4 ml. of freshly isolated motile cancer organisms killed mice in less than 24 hours. It would seem that a strong toxin was present in such cultures. When sublethal numbers of motile rods were inoculated, they broke up into minute bodies which invaded both cytoplasm and nucleus of the host cells. Animals given experimental rabbit antiserum, prepared either against pure cultures or against tumor extracts, showed a different picture. Tissue cells were not invaded, fewer organisms were present and were often seen as ring forms. That in some cases the protection was only partial was indicated by the budding out of acid-fast rods from the rim of some of the rings.

What is the importance of recognizing these various forms of mycobacteria? Twenty-five years of observation and experimentation with various pathogenic mycobacteria have led me to conclude that atypical forms can serve the physician as signposts (1) in the diagnosis of doubtful cases, or cases in which typical forms are not found, and (2) in prognosis, as an indication of how a patient is responding to treatment. Ring forms and other globoidal bodies appear to indicate increased host resistance, whereas the preponderance of viruslike bodies and rods—especially motile rods—would seem to show lack of, or decreased, host resistance.

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A SYMPOSIUM ON
SOMATOTHERAPIES IN PSYCHIATRY

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Insulin Coma Therapy

Clinical Studies on Anticancer Agents, 1952-53

*John R. Sampey, Ph.D.**

GREENVILLE, S. C.

Several surveys of clinical investigations on anticancer agents have been made recently by the author.[80–82] The present paper covers the treatment of patients during 1952–53 without repeating any of the studies in earlier reviews.

I. INORGANIC AGENTS

Radiogold. Studies with Au^{198} led all current studies on the clinical use of radioactive isotopes in the treatment of neoplasms. James et al[52] reported radiogold seeds effective against carcinoma of the tongue, melanoma, and other neoplastic growths. Andrews[3] obtained good results by interstitial injections of Au^{198} directly into prostatic carcinoma; he also found effective intracavitary injections of the isotope in patients with fluid in the pleura or peritoneum, and he used intravenous injections for chronic myelocytic or lymphocytic leukemia. In two further studies,[4, 5] Andrews et al gave intraperitoneal and intrapleural injections for effusions associated with neoplasms. Knisely and Andrews[59] determined from autopsy studies that radiation damage to lymphosarcoma, squamous sarcoma, and adenocarcinoma of the breast, ovary, stomach, etc., was limited to superficial zones when injected directly into the cavity to be treated. Rose et al[77] employed intracavitary and intraperitoneal injections of Au^{198} to help patients with ascites. King et al[57] reported intracavitary administration of radiogold produced relief of symptoms in patients with pleural effusions and ascites associated with malignancies. Flocks et al[43] noted a good response with radiogold therapy against prostatic carcinoma.

Radioiodine. Bierwaltes[15] noted that 16 patients with thyroid carcinoma, or 8 per cent of those given surgery, x-ray therapy, and I^{131} treatments, showed unequivocal improvement, and 3 were completely cured. Dobyns et al[29] reported no cases of sarcoma developed in 400 patients treated with I^{131} at the Massachusetts General Hospital. Pochin et al[74] found thyroid carcinoma responded to iodine therapy. Rawson and Rall[76] observed that 4 out of 22 patients given I^{131} for thyroid tumor showed marked resolution of pulmonary lesions, and that 6 more had lung tumors shrink.

Radioarsenic. Block et al[17] found from biopsies on the lung and spleen of leukemic patients that As^{76} caused some cellular destruction.

Radiostatine. Bruner[20] reported the clinical use of At^{211} on thyroid neoplasms.

Radiolanthanum. Lewin et al[62] studied the therapeutic effects of La^{140} on leukemia.

Radiophosphorus. Erf[34] used P^{32} on blotter paper attached to neoplastic growth of the skin. He also administered it orally or intravenously for leukemia or polycythemia vera with good results.

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TEM. Triethylenemelamine is one of the most widely used of organic nitrogen compounds in the therapy of leukemia and allied neoplasms. Silverberg and Dameshek[92] reported remissions in 30 per cent of patients with Hodgkin's disease, and found that TEM was effective against leukemia also. Wright et al[109] and Rundles and Barton,[78] Paterson et al[72] and Bayrd et al[11] reported improvement in patients with leukemia and Hodgkin's disease following oral administration of the drug. Kravits et al[60] gave the drug orally and intravenously for leukemia and lymphomas. Karnofsky et al[54] caused temporary clinical improvement in patients with Hodgkin's disease, lymphosarcoma, chronic lymphatic and myelogenous leukemia, and mycosis fungoides by giving doses of TEM. Gellhorn et al[46] described the improvement of 54 patients with disseminated neoplasms, including lymphomas, chronic leukemia, and lung carcinoma, following TEM therapy. They reported the drug less toxic than HN2. Loeffler et al[64] compared single doses of HN2 intravenously and TEM orally in patients with carcinoma of the lung, colon, etc. Ellison et al[32] employed TEM to bring relief to patients with polycythemia vera.

Nitrogen Mustards. Nitrogen mustards have been widely used also against a variety of neoplasms the last two years. Mention has been made of the treatment of different carcinomas by HN2. Several reports have been concerned with the intra-arterial administration of nitrogen mustards: Sullivan and associates[99] used a simplified catheter technic against Hodgkin's disease and lymphosarcoma; Cromer et al[25] caused carcinoma of the cervix to regress by intra-arterial administration of mustards; Bonner et al[15] noted subjective and objective improvement in 44 per cent of 16 patients when they employed cannula tubes for bladder, leg, and genital neoplasms. Barberio et al[8] combined successfully the intra-arterial administration of mustards with Aureomycin against various adenomas; Bierman et al[13] increased the effectiveness of HN2 therapy by slowing the blood flow through various types of neoplastic lesions (arterial infusion of HN2).

Weisberger et al[105] gave l-cysteine hydrochloride intravenously to patients with Hodgkin's disease prior to HN2 administration and noted that larger doses of the mustard could be tolerated. Zimmerman et al[110] helped 10 of 15 patients with liver lymphomas by intravenous injections of HN2. Deuschle and Wiggins[28] employed nitrogen mustard in the management of 2 pregnant patients with lymphoma. Levinsky and Kern[61] reported no improvement in 1 patient treated with mustard for fluid, electrolyte, and protein depletion secondary to the bronchorrhea of pulmonary adenomatosis.

TEPA. Farber and associates[38] reported on the carcinolytic action of triethylenephosphoramide, given orally or intravenously to patients with Hodgkin's disease, malignant melanoma, and other neoplasms. Sykes et al[100] obtained similar results with TEPA and diethylenephosphoramide. Downing et al[31] found TEPA helped patients with melanoma.

Guanazolo. Colesky et al[23] reported the antineoplastic effects of guanazolo in patients with disseminated neoplasms after the drug was given intramuscularly or parenterally. Wright et al[108] noted the improvement of 2 patients with Hodgkin's disease following the oral administration of the drug.

Urethan. Alwall[2] recorded that a patient with multiple myeloma was subjectively quite well for three and one-half years of urethan treatment, but that after two and three-quarter years the sedimentation rates gradually increased and anemia and leukopenia prevailed.

6-Mercaptopurine. 6-MP tablets were given 107 patients with leukemia and allied diseases by Burchenal et al;[22] 15 of 45 children with acute leukemia, Hodgkin's disease, etc., showed good clinical and hematologic remissions, and another 10 some remissions; 35 patients with lymphomas, carcinomas, and sarcomas showed no definite improvement.

Dihydrotriazines. Farber et al[39] found monochloro–dihydrotriazines and dichloro–dihydrotriazines showed antileukemic properties in children.

Nitrofurans. Friedgood et al[44] obtained marked regression of testicular tumors (seminomas) following nitrofuran therapy.

Glucosamine. Marlow and Bartlett[66] recorded that oral doses of glucosamine did not influence 1 case of acute leukemia, 1 with chronic myelocytic leukemia, 2 with chronic lymphocytic leukemia, and 1 with acute histomonocytic leukemia.

III. FOLIC ACID ANTAGONISTS AND ANALOGS

Folic acid antagonists and analogs were widely used in clinical studies of neoplasms in 1952–53. At the second conference on folic acid treatment of leukemia[24] favorable results on the clinical use of these agents were reported by Bethell,[12] Burchenal,[21] Farber,[37] Heinle,[50] Pierce,[73] Sacks,[79] Stickney,[95] and others. The limitations of the therapy were also brought out.[26]

Schoenbach et al[84] reported 5 of 8 patients with acute leukemia showed improvement after treatment with aminopterin and amethopterin. Sawitsky et al[83] recorded one complete remission and five favorable responses to oral doses of aminopterin in acute leukemia. These same investigators noted 1 of 11 leukemic patients improved after intramuscular injection of aminoanfol.

Kingsley-Pillers et al[58] tested 16 children with corticotropin and cortisone after their leukemic condition showed no further response to folic acid therapy. Ten of these had good clinical and hematologic response. These investigators gave 6 leukemic children amethopterin after they failed to show improvement from hormone therapy, and 3 had good response. Branche et al[19] treated 10 patients with gastrointestinal cancer with dichloroaminopterin; no clinical benefits were noted, but they suggested further testing with other derivatives.

IV. HORMONES

Estrogens. Estrogens continued to be used widely in the hormonal treatment of neoplasms. Breast cancer responded to a number of estrogens.[27, 47, 63, 65, 68] Emerson et al[33] employed diethylstilbestrol, sodium estrone sulfate, diethyl ether of stilbestrol, stilbestrol, monomethyl ether of stilbestrol, and ethinyl estradiol to cause regression in mammary carcinoma. Escher[35] induced subjective and objective improvement in advanced mammary cancer with diethylstilbestrol, estrone sulfate, ethinyl estradiol, and estradiol dipropionate. Douglas[30] advocated stilbestrol dipropionate for carcinoma of the breast in women five or more years past menopause.

Estrogens have also been used extensively in advanced cancer of the prostate.[6,7,42,67] Scott[58] employed stilbestrol therapy followed by radical perineal prostatectomy. O'Connor and Sokol[71] noted a larger survival in 50 patients with prostatic carcinoma given the estrogen TACE.

Nieburgs[70] recorded that 5 of 7 patients with carcinoma of cervix who received excessive doses of diethylstilbestrol showed no remains of cancer in biopsy specimens. Barnes and Rothchild[9] noted that 12 patients with cervical carcinoma who received irradiation therapy, followed by progesterone treatment for 9 days, had a softening of half the tumors, and one-fourth the post-treated cervical smears were negative.

Androgens. Androgen therapy in cancer of the breast received much attention during the last two years.[33, 35, 63, 68] Segaloff et al[88, 89] induced regression in 8 of 27 patients with mammary carcinoma by the administration of methyltestosterone orally or by buccal route. Earlier Segaloff et al[86] had noted two regressions in 24 patients with breast cancer following treatment with methylandrostenediol, but found that androstenediol induced no regressions or well feeling in 21 patients.[87] Kasdon et al[55] reported methylandrostenediol improved 30 of 44 patients in the palliative treatment of breast cancer. Farrow et al[40] induced regressions in patients with advanced mammary carcinoma by intramuscular injections of androstane-17-(β)-ol-3-one. Escher[36] found dihydrotestosterone therapy as effective in 45 patients as testosterone in treating mammary carcinoma. Douglas[30] recommended testosterone for women not more than five years past menopause who had advanced breast cancer. Baker[6] condemned the use of this hormone for men over 50 suffering from advanced cancer of the prostate. Graham and Graham[48] enhanced the effectiveness of radiotherapy in cancer of the uterine cervix by testosterone propionate given intramuscularly, and alpha-tocopherol given similarly or orally.

ACTH. Block and Jacobson[16] noted that two thirds of 21 leukemic patients treated with ACTH or cortisone were benefited. Adams et al[1] recorded remissions in 5 out of 10 patients with leukemia following similar treatments. Fenninger et al[41] used ACTH and cortisone to regress lymphosarcomas and leukemia, while Pierce[73] obtained good results in the therapy of leukemia with folic acid antagonists and ACTH. Soffer et al[93] described a striking regression in 1 patient with a malignant thyroid tumor following ACTH therapy.

Cortisone. The treatment of leukemia with cortisone and ACTH has just been noted.[1,16,41] Kingsley-Pillers et al[88] treated 16 children with acute leukemia with cortisone and corticotropin after no further improvement was noted from antifolic acid therapy. Ten of these had good clinical and hematologic response. Straus et al[96] studied the effect of cortisone in patients with advanced Hodgkin's disease. Subjective improvement was noted in 7, and 3 had their temperature reduced to normal, but the investigators recorded only one regression and no true remissions. Siltzback[91] gave cortisone orally and intramuscularly to 13 patients with sarcoidosis, and noted subjective and objective improvements in all. Sullivan et al[98] caused skin lesions of sarcoidosis to regress temporarily by giving cortisone orally or by local injection of hydrocortisone. Karnofsky et al[53] infiltrated skin lesions of Hodgkin's disease with 11-alpha-hydrocortisone, but did not note any inhibition of lesions.

V. MISCELLANEOUS

Hemisulfur Mustard. Seligman et al[90] gave patients with prostatic carcinoma intravenous injections of 2-chloro-2'-hydroxydiethyl sulfide. He also noted improvement in 8 patients with ascites from peritoneal carcinomatosis.

Podophyllin. Sullivan[97] recorded the failure of podophyllin in the treatment of cutaneous carcinoma.

Polydine. Von Jelinek[103] reported that polydine did not alter the course of 12 patients with carcinoma and sarcoma.

Myleran. 1,4-Dimethanesulfonyloxybutane was given orally by Galton[45] to 19 patients with chronic myeloid leukemia. All responded but 9 relapsed in six months and 8 had remissions from 21 to 6 months.

Alpha-peltation. Greenspan et al[49] obtained transient regression in patients with carcinoma and lymphoma by intravenous injections of alpha-peltations.

Yeast. Protti[75] reported that intravenous injections of yeast caused considerable disintegration of various types of neoplasms.

Aureomycin. Bateman et al[10] recorded improvement in advanced cases of cancer from parenteral aureomycin therapy. Barberio et al[8] caused various types of adenoma to regress by the combination of Aureomycin and nitrogen mustard given intra-arterially.

Monobenzyl Ether of Hydroquinone. Kelly et al[56] noted that the drug had no effect on the growth of malignant melanoma.

Infectious Diseases. Huth[51] noted remissions of leukemia and malignant tumors following infectious pneumonia, erysipelas, etc. Bierman et al[14] described temporary remissions in 10 leukemic children after streptococcus, staphylococcus and other infections. Taylor[102] caused temporary regressions in acute leukemia with intramuscular injections of glandular fever. Nauts et al[69] also recorded a number of remissions in neoplasms following bacterial infections, either spontaneous or induced in patients.

Egypt 101 Virus. Southam and Moore[94] caused carcinoma to regress in 9 of 24 patients by intravenous or intramuscular injections of Egypt 101 virus.

Tumor Extracts. Weiss[106, 107] caused cancer patients to feel stronger, have more appetite, and gain weight by giving extracts of malignant tumors intramuscularly.

Spleen Extracts. Watson[104] noted improvement in patients with mammary cancer, skin cancer, and fibrosarcoma following intravenous injections of spleen extracts.

Krebiozen. Szujewski[101] reported Krebiozen ineffective in all patients treated.

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PSYCHOPATHOLOGY FOR THE GENERAL PRACTITIONER

The Reproduction of Psychosis in Science Fiction

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It has rightly been considered one of the important discoveries of dynamic psychology that different manifestations of human behavior spring from the same sources. These may motivate the individual unconsciously. Significant similarities are found among such diverse productions as dreams, parapraxes, neurotic symptoms, and also the hallucinations and delusions of the psychotic, and those imaginative creations that are art and literature. In fact, this awareness of the basic unity of all these phenomena is often the indispensable key to their understanding, since their surface appearance is frequently so very different from their motive force. It is the aim of this paper to explore the connection between certain specific pathologic productions and a specific literary genre—science fiction—and to relate both to significant trends of our culture.

We may supplement the dynamic concept of the relationship between different forms of behavior by introducing a morphologic concept: we shall call those manifestations morphologically similar which have the same content but differ in their relationship to consciousness. Example:

> Gone are the days when my heart was young and gay,
> Gone are my friends from the cotton fields away,
> Gone from the Earth to a better land I know—
> I hear their gentle voices calling, "Old Black Joe!"
> I'm coming, I'm coming, for my head is bending low—
> I hear those gentle voices calling, "Old Black Joe!"[1]

Obviously, when a real person in his waking state hears the gentle voices of his dead friends calling his name, this is a hallucination and may be indicative of psy-

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chosis. It does not necessarily have this connotation in poetry; though the content is the same, the relationship to consciousness is different. To Old Black Joe, in the song, hearing the gentle voices may mean just a figure of speech. What it means to the poet and to the audience is a different question again. The inner relationship between a literary production and its morphologic equivalent in psychopathology is not a problem of definition but has to be explored on the basis of facts.

We can postulate several morphologic categories and can see how they apply to science fiction.

1. Realimorph: A type of literary production that depicts chains of events of the same nature as those actually observed in reality. This is of course the category into which, by and large, all realistic and naturalistic novels, plays, short stories, etc., are bound to fall. Science fiction by its very nature can not be expected to exhibit marked features of this type.

2. Somniomorph: Literary productions depicting events of such a nature, and connected in such a manner, as they typically occur in dreams. Much of the work of Kafka, for instance, is of this quality. One might expect to find a great deal of it in science fiction, but this expectation is not fulfilled.

3. Egomorph: Attributing an unrealistically exalted role to the hero, thus reflecting the self-aggrandizement that is characteristic of daydreams and of fantasies of the neurotic. This is, of course, widespread in various literary categories and of the very essence of "popular" literature. Science fiction has its share of this, but hardly more than comparable literary genres.

4. Schizomorph: Literary productions that parallel the productions of the schizophrenic (especially the paranoid schizophrenic) in such a manner that a person who would believe that the events depicted in those stories could happen in real life—and more specifically, that they could or did happen to him—would on the strength of that be diagnosed as schizophrenic. Old Black Joe's voices are an example of a schizomorph turn of phrase, but it is very rare in literature to find a schizomorph motif except one as sketchy and fleeting as this.

Elaborate schizomorph productions are, however, surprisingly prevalent in science fiction.

We shall attempt to illustrate this, after a brief review of the general background.

The development of science fiction has kept pace with the rise of science as a major force in society that has a growing hold on popular imagination. Like science itself, it can be traced to the ancient Greeks. More than a thousand years of silence followed. Modern science fiction begins—appropriately—in the early seventeenth century. It developed slowly at first, but at a growing rate since the late nineteenth century, when such writers as Jules Verne and H. G. Wells brought it a wide appeal. It has achieved a place in public consciousness since World War II. This is chiefly an American development; in science fiction, the United States leads the world.

Being of such recent vintage as a full-fledged literary category, science fiction has so far had little scientific attention. Its very definition is poorly established. We may consider as science fiction all those works of literature (other arts, such as films and cartoons, can be neglected here) in which a fictitious scientific or technologic discovery or invention is an essential feature of the content.

We may also be guided by usage and consider as science fiction those works that are so labeled by their authors. This can be recommended on the ground that science fiction has become, sociologically speaking, institutionalized: the bulk of it makes its appearance in special science fiction magazines and anthologies, works of science fiction are classified by libraries as such, etc.

The reservoir of fictitious innovations into which science fiction authors can dip for their plots is of course inexhaustible. Which of these choices have they favored?

In some cases they have selected innovations toward which science was actually working. Some features of the atomic bomb were anticipated in science fiction almost half a century before Hiroshima.[2] An anticipation that astounds by its relative accuracy (including, as it does, the term "atomic bomb," some of the underlying scientific principles, and a keen appreciation of the resulting problems of world politics) was published years before the Manhattan Project started.[3] However, these are rare instances.

The impression has been spread by some science fiction literature and has gained rather wide currency, that science fiction is the pace setter for science—as though we should expect to read of a new development in fiction today, in news reports tomorrow. This is not borne out by the facts, nor is there any reason why it should be. The business of science fiction is not prediction (which is the business of science) but imagination. It is perfectly legitimate for a science fiction writer to allow his fantasy free play even to the extent of describing a discovery—e.g., of dinosaurs surviving in a deep cave[4]—that is clearly improbable or indeed impossible.

Several motifs are found with paramount frequency in current science fiction. Three of these are of special interest to us:

A. SPACE TRAVEL

This is of course the most obvious and best known science fiction motif; so much so that science fiction is frequently—but erroneously—identified as the literature of space travel. It has often been tacitly taken for granted that the preoccupation of science fiction with space travel reflects the shrinking of our world, which has left us with no other "frontier," and that it foreshadows the actual "conquest of space." Neither of these assumptions contains more than a grain of truth.

Much scientific work is going on that holds the promise of technologic achievement in the near future; it can not be a coincidence that science fiction has pounced just on the dubious motif of space travel, while neglecting advances in other fields (e.g., conquest of disease). As far as the "shrinking" of the Earth is concerned, it has by no means made it indispensable for the science fiction writer to place his story outside of the Earth. Apart from the possibilities of displacement into the future and into subterranean locations, there is room enough even on the surface of the land. One contemporary novel that utilized this possibility[5] has been so successful that "Shangri-La" has become a common word in the English language.

If science fiction writers nevertheless insist on placing their stories in extraterrestrial settings, it is clear that they do so by choice rather than from necessity. In fact, some works mention space travel when the plot really does not require it. In a story

which deals exclusively with a fictitious method of repairing brain damage, the fact that the hero was a much sought-after doctor is illustrated by stating of one of his patients that "a spaceport engineer, he had been browned with the sun of several planets."[6] One odd little story, which in all seriousness can best be summed up by saying that it shows the workings of the Oedipus complex in colonial administration, is set on a small planet when it could just as well have been set in a remote colony on Earth (nobody in the story travels anywhere but on that one planet).[7]

Episodes of space travel are by no means rare in the imaginings of the mentally ill. So far, only isolated reports[8] can be found in the literature, perhaps because records of the contents of psychotic productions are infrequent in general and are especially rarely made where the production seems to deal with abstract material rather than with the patient's body or his interpersonal relations, two fields to which greater attention has been given. Tausk's classic paper on certain psychotic ideas[9] will interest us in another connection.

One of the oldest and most elaborate case studies relating to space travel is one in which a Swiss psychologist recorded his observations of a medium (Hélène Smith) over a period of years.[10] Miss Smith held séances in which she believed she communicated with the spirits of the dead. She became convinced that she had in a former life been Queen Marie Antoinette of France, and before that an Indian princess. Outside of the séances she led a normal life.

In 1892 a book on Martians was published[11] which created a sensation that gradually reached Geneva, where Miss Smith was living. On November 25, 1894 she began to have sensations which she interpreted as actually travelling to and from Mars. She saw scenes that her familiar spirit informed her "were actually passing on Mars." She received messages from Mars, talked in Martian language, wrote down an alphabet of Martian letters, and furnished a fragmentary Martian-French dictionary. A "simple family fête" on Mars was described by her as though she were watching it on television:

> Then come two men in long white trousers with a black sash. . . . They carry ornamented trays, and passing in front of each table they place square plates upon them, with forks without handles, formed of three teeth an inch in length; for glasses they had goblets like tea cups, bordered with a silver thread. Then they brought in a kind of basin a cooked animal, resembling a cat, which is placed before Astané who twists it and cuts it rapidly with his fingers, tipped with sharp silver tips; square pieces are distributed among the guests on square plates with furrows around the edges for the juice. Every one is filled with a wild gayety. Astané sits at each table in succession, and the girls pass their hands through his hair. New plates are brought, and pink, white, and blue basins tipped with flowers. Then the guests wash their hands at little fountains in the corners of the room . . .

Reviewing this effusion, Flournoy remarks judiciously:

> One would say that it was the work of a young scholar to whom had been given the task of trying to invent a world as different as possible from ours, but *real*, and who had conscientiously applied himself to it, loosening the reins of his childish fancy in regard to a multitude of minor points in the limits of what appeared admissible according to his short and narrow experience.

Much of this critique would apply so exactly to descriptions of events on other heavenly bodies in modern science fiction that the morphologic similarity can be considered complete.

Since extraterrestrial aviation, however imminent it may be, has not been invented yet, fantasies of space travel must needs be projected into the future—unless contact with reality is abandoned to the extent to which "Miss Smith" did so. The "schizophrenoid" young patient who has been described as the "space child" solved the problem by imagining a "time machine."

The primary purpose of this device is to carry him into the future in which space travel will be possible, but it is only one step from there to reverse gears as it were. He has taken the step:

> With this time machine it would be possible to travel back into history and to change things. . . . For instance, if an emperor in Germany was shown to be responsible by the study of history for some of the warlike atmosphere of the present age, this time machine would allow us to go back to that age and kill the emperor before he had a chance to be influential.[12]

This may of course be considered an imitation of H. G. Wells' famous time machine. A much closer correspondence exists with some more recent and less well known science fiction stories.

The plot of "Untitled Story"[13] is essentially this: Flaherty, the Mayor of Chicago, has cancer. He buys "cure-all water" from Lehman, the villain of the story. The vial turns out really to contain an elixir—brought into our time from a future century—which cures cancer and in fact prolongs the life span to one thousand years. Cathy, the heroine—herself a time-traveller from the future—explains it to Don, the hero-detective, thus:

> Lehman is a member of what you would call a political party, but not a legally recognized one. By traveling into the past he thought to change it enough so that his party would be in power in the far future. . . . If Flaherty lived long enough he would back a certain candidate for senator. This person in turn would become president. A very poor president, Donald. A tyrant. And the past would be altered sufficiently so that Lehman would be our ruler in the future.

This is a good deal more complicated than the Space Child's fantasy of killing a German emperor. Yet the analogy between the literary and the psychopathologic production is striking. Fairly similar ideas have been expressed in other science fiction stories, including one that will interest us in another connection.[14]

It is noteworthy that the familiar motif of the hero being pursued by the cohorts of the villain has undergone an odd modification. As in so many thrillers, the detective in "Untitled Story" is chased over roof tops, fired at from a variety of weapons, slugged, tied to a chair, drugged, left to die—only to kill the villain and to win the heroine in the end. But his would-be murderers are an unusual lot: a "blind" newsboy who actually merely wears grey contact lenses; the Mayor's butler who pretends to be incurably ill; the cop on the beat; the grocery clerk; the elevator man; a pushcart peddler—in short, all the men with whom the hero makes casual contact, and all of them turn out to be time-travellers from the future who have disguised themselves.

In other words, all the men whom the hero encounters on his way home from his (heroic) work turn out to be something different from what they seem and to be there for the sole purpose of watching and eventually murdering him.

It is true that this may be classified as an elaboration of the usual motif of the

chase; just as the delusions of the paranoid may be considered as a modification of the fears of a man who has reasons to believe that the police is after him.

B. REMOVAL FROM COMMUNION WITH THE LIVING

A motif of much greater complexity than space travel, both within itself and in its morphologic counterparts, is that of the "last man:" an individual finds himself as the only one left living in a deadened world after a catastrophe has annihilated everybody else.

Now in this "age of anxiety" many people think that such a cataclysm may indeed be upon us any day. That science fiction should elaborate on this would therefore seem a quite realistic reflection of a widely held belief. Just as with space travel, however, closer scrutiny shows that this justification is a rationalization. Two considerations in particular will demonstrate this.

For one thing, if mankind is destroyed, the chances are that either nobody will survive or that there will be an indefinite, oddly assorted number of survivors. The chance that just one person would survive is obviously infinitesimally small. The chance that two persons should survive and that they should be of opposite sex and both of mating age, is, if possible, even smaller.

It is understandable that the idea of annihilation without survivors has not particularly attracted the writers of fiction, since there would be no one to tell the tale and no plot could be carried much farther. The motif that a motley group survives has been employed in several works. In one of the few existing scientific studies of science fiction[15] this hypothetic group has even been given a name ("the utopian remnant"). However, the writers who have utilized this version of the motif are by and large not closely identified with modern science fiction. This applies to several stories of epidemics sweeping over the globe and killing off most people,[16, 17] as well as to a larger number of stories in which the same effect is achieved by atomic war. The bulk of science fiction writers, however, prefer, in open disregard of the laws of probability, to let one person or one well-matched couple survive.

Secondly, the motif of the last man by no means made its debut with the splitting of the atom, but flourished already when there was no reason to believe that a universal catastrophe could happen. The use of the one-survivor motif in classical literature is splendidly exemplified by Coleridge's "Ancient Mariner," that of the surviving couple by Deukalion and Pyrrha in Greek mythology.

Far from being a byproduct of atomic fission, the "last man" motif grows from the fertile soil of unconscious drives. It can indeed be found in spontaneous fantasies, which are not contrived for an artistic purpose. It is found in dreams. It is found in the fantasies of children and adolescents. Not by any means merely in the fantasies of the cruel and the spiteful, of those who, with a notorious Roman emperor, consciously wish that all mankind should have but one neck so that it could be cut with one stroke. No, fantasies of this sort are reported with fair frequency in autobiographies (let us remember that only persons with a penchant to introspection write autobiographies), and actually by some people whose conscious adult life was marked by good will and gentility. Two examples may do for many which could be given.

A. A. Milne, author (especially of children's books), reports a day dream or fantasy involving himself and his brother Kenneth:

> Our dream was, quite simply, that we should wake up one morning and find that everybody else in the world was dead . . . . This sounds callous, but it was really no more than a variation of the desert-island dream which every small boy has. It just didn't seem possible to get a desert island . . . . But it *was* conceivable that God, who had done something on these lines more than once, should destroy everybody in the world but Ken and me. And even if He were not doing it directly, or with any great enthusiasm, yet (as it were, in spite of Him) disasters did happen, a plague might fall upon the people, and everybody might die. (Except Ken and me) . . . . Yes, it sounds horrible put like that . . . . in a week we would wish them all alive again. But oh! to wake up one morning and find that everybody was dead—except Ken and me. It was the freedom of the sweet-shops which we wanted most. Never to have to pass a sweet-shop again, but to be able to step in confidently over the body of the dead proprietor—that was Heaven.[18]

Jane Addams, the eminent social worker, says: "I dreamed night after night that every one in the world was dead excepting myself. . . ."[19]

These are perhaps the growing pains of the humanitarian mind. In those cases where the underlying conflict is not solved in the process of growing up by the victory of sublimation or other ego defenses, but where it breaks forth in psychosis, the "last man" motif is often modified. Reversal of the roles is not infrequent. Quite understandably so: if the individual's basic feeling is isolation from the world of other living beings, the difference is not too great whether it is conceptualized in the way that he is alive while all the rest of the world is dead, or vice versa, or whether the isolation is achieved by removal in time or space. I am not likely to forget the client who missed an appointment and responded to a follow-up letter with a nicely typed note that began thus:

> Dear Mr. Plank: I have to apologize for not having written to you earlier. The reason is that I was dead. However, I have been brought back to life by the grace of God and the United States Supreme Court.

Every practitioner who deals with schizophrenics is, of course, familiar with this type of delusion. The reversed delusion is perhaps more often hinted at than elaborated. The connotation of the feeling that the world around the patient is not really alive—a chilling emotion characteristic of different forms of psychosis—is discernible in complaints like this one recently made to me:

> Whenever I come to your office, I have to walk through these crowds downtown. They bother me. I often wonder: Where do they all come from? Where are they going?

C. INFLUENCING MACHINES

Extreme isolation in fantasy may provide a peculiar sort of satisfaction; if achieved in actual fact, it may be found intolerable. It is helpful for our purpose to consider that the schizophrenic has to defend himself against a fundamental difficulty—his inability to form meaningful interpersonal relations—and that in the paranoid type the defense succeeds by erecting a system of delusional relationships that take the place of the relationships that do not exist in reality. We are not stating anything new but are merely recapitulating in order to compare this better with fictional

equivalents, if we say that three types of delusion are the mainstay of the structure: delusions of grandeur, of persecution, and of influence.

Since delusions of grandeur and of persecution are misinterpretations of human conduct—a field of behavior notorious for its vagaries—they do not necessarily run into obvious and crass contradiction to reality. The dividing line between the peculiar emphasis that forms the morphologic correlate of what we have called egomorph on the one hand, and delusions of grandeur and persecution on the other hand, is not sharp. The appearance of such ideas in science fiction, striking though they may be (as in the case of our time-travelers) is therefore of limited value in demonstrating the schizomorph character of this literary genre.

It is different with the delusions of influence. These do not merely misinterpret human behavior, but they disregard laws of extrahuman nature, which leave less leeway. The point is quickly reached at which it becomes glaringly clear that the discrepancy between belief and reality is irreconcilable. The following two case observations illustrate delusions of influence of different type and degree of severity, with fairly typical admixture of elements of delusions of grandeur and persecution.

Case of J. S.: A male in his early thirties was hospitalized with a diagnosis of schizophrenia, paranoid type (although his behavior at times was more reminiscent of the catatonic). One of his complaints was that when he served as a soldier in Europe, General Eisenhower had taken his heart out and replaced it by two artificial hearts. The patient was given electric shock therapy, to which he submitted willingly, showing a fairly accurate understanding of the nature of the treatment. Like many other patients, however, he felt muscular discomfort as the result of the treatment. He accounted for this by elaborating his delusion: his two artificial hearts, he claimed, had originally been connected by General Eisenhower by means of a steel spring. Shock therapy had induced an electric current in the spring which had torn it loose, so that the spring wandered around in his body, causing his aches.

At this time the presidential campaign of 1952 got under way. The patient followed the candidates' itinerary in the newspapers. Whenever Mr. Eisenhower was scheduled to appear in a city near the hospital, the patient implored the social worker to contact the general so that he would visit the hospital and fix the spring connecting the patient's hearts, since the hospital doctors had proved incapable of doing so and apparently no one else could do it either.

Even though this is a case of passive delusion of influence (the patient believes that he has been influenced and does not claim that he can influence others), delusions of persecution are not especially systematized in this rather passive, slightly feminine young man. The marked delusion of grandeur appears vicariously, in the guise of claimed consideration from the great.

It is worth noting that J. S.'s delusion combines old and new motifs. The motif of the artificial heart as such is old. It can presumably be traced back to the concept of the migratory soul.[20] In its developed form it is found in Hauff's fairy tale (or rather, legend with a moral) "Das kalte Herz," written more than a century ago.[21] This story describes how a demon buys up people's hearts and places them in jars in his den where they keep on ticking like so many watches, while he replaces each heart with a stone that he puts in the man's chest (with the expected effect on the man's behavior). The artificial heart here in Hauff's tale is, characteristically, not an artifact but just a stone; there are no moving parts to get out of order. This elaboration found in J. S.'s complaint is more modern—and closely akin to science fiction.

Case of F. T.: During the acute stage of schizophrenia, this college-trained engineer suffered from auditory hallucinations, which he referred to hidden radios and similar contraptions. His symptoms subsided during a year of hospital treatment; he was eventually discharged, and a follow-up study a year later showed that he was steadily working and apparently well adjusted. Shortly before his discharge from the hospital, he expressed his concern about the possibility that his mind may be read and influenced, explaining his concept as follows:

It is well known that the electroencephalograph, operated by means of electrodes attached to the outside of the skull, records electric currents which are specific for certain areas of the brain. It is also well known (so the patient stated) that mental processes are so localized that specific thoughts, feelings, and memories have their seat in specific cells—in such a manner, in fact, that a certain mental content corresponds to each brain cell and vice versa. It is known, furthermore, that investigators at Tulane University and other places (the research at Tulane had been mentioned in the *New York Times* weekly science news summary shortly before this conversation took place) have inserted wires into definite loci in the brain for the purpose of producing specific electric phenomena in them.

It would be possible, then, to identify the function of each brain cell and to construct a modified electroencephalograph operating by way of electrodes leading through the skull to specific brain cells; this machine would record the current of each cell. For instance, clamp an electroencephalograph on a patient, direct an electrode into the cell in the brain whose function is sexual excitement, show the patient the picture of a naked woman, and read his feelings from the jagged line which the electroencephalograph will record. In addition to thus reading the patient's mind, it will equally be possible to modify his thoughts and feelings by directing electric currents to specific brain cells which have been identified as the seat of the mental process that is to be changed; these currents could be made to stimulate or inhibit the action of the cells concerned, as desired in the individual case.

The patient said that he was not sure whether the hospital already possessed such a machine. He pointed out various apparatus, which he had seen on the ward and the purposes of which baffled him, and referred to various hospital practices which indeed amounted to keeping information from the patients. He thus indicated that he thought it probable that such a machine had already been constructed and had secretly been used on him.

Perusal of almost any number of a science fiction magazine will yield plenty of parallel material. For example, in "Tyrants of Time"[14] the hero is attacked by an as yet unidentified girl.

> As Tedor fell, the woman's face etched itself into his memory. It spun into giddy unconsciousness with him and his last thought was that he would never forget it.

It is important to know who she is, so he reports to his superior, Ruscar, who proceeds as follows:

> Ruscar led Tedor to a chair, told him to sit down. Soon Ruscar had clamped an electrode to the side of Tedor's head, plugging the wire which led from it into the wall. 'Let's concentrate on this girl you found in Fornswhitte's place.' Tedor nodded, found it ridiculously easy. Moments later, a sheet of paper popped out of a slot in the wall. Ruscar retrieved it, stared at the sketch of a beautiful face.

The picture which has thus been extracted from Tedor's brain is sent to the central file, and after five minutes the corresponding rogues' gallery picture appears; identification is completed. It is that easy—"ridiculously easy."

It is perhaps not a coincidence that this marvelous device is operated by Ruscar, who is finally unmasked as the villain of the story. Those uncanny inventions are not seldom attributed to evil men. A fair number of them are psychiatrists.

Dr. Waterson in "Mind Alone"[22]

> was one of the new electronic psychiatrists. He seemed to have grown a little electronic himself; he hummed like an electric motor as he worked, his little black eyes glittered like nuclei, and his black hair perpetually stood on end as if charged with electricity.

What do "electronic psychiatrists" do?

> So they systematically destroyed her knowledge. . . . the next thing to go was her entire personal experience. All her memories of every event in her life were cleared away like so much rubble. She didn't know who she was or anything she had ever done. . . . The process, however, wasn't done with kindness, consideration and loving care. Since there had to be pain, they used it for conditioning. To make sure the conditioning was effective, they did nothing about quite a lot of pain that could have been avoided. . . . After all this, they removed the personal memories she had begun to build up again since the last rape of her mind, and left everything else alone. They tested her, and were pleased.

Quite another type is Dr. David Mantell, the psychiatrist in "Discontinuity."[6] A benefactor of mankind, he has at first less reason to be pleased. True, he "could take apart the brain of a man, cell by cell, and reconstruct it in the image of a living human being." By inventing the "Mantell Synthesis," he had

> provided the medical world with its most brilliant technique in thirty centuries of its history. . . . With one sweep he eliminated the centuries old butchery of lobotomy and topectomy which had maimed hundreds of thousands in its long fad.

The operation is lovingly described in detail:

> David held the helmet in his hands, its hundred spiny probes a terrible weapon to hurl into a man's face if he had to do it. . . . By electroencephalograph they positioned the helmet with exacting care. Carefully, the hundred or more probes, scarcely a dozen molecules in thickness, were screwed down, penetrating the skull into precise loci in the brain structure. . . .

Our patient F. T. could hardly have done better.

But alas, what good does all this do?

> To date, his experiments had resulted only in intensifying the very conditions they were designed to heal. In a hundred cases of extensive brain damage, his process had restored life, but only in varying degrees of hopeless aphasia. At first the public hailed the magnitude of his stride, then, revolted by the horror of his failures, they had turned against him with a mighty clamor.

Naturally, this merely serves to make the final triumph that much greater. The story ends with a strong hint that the Mantell Synthesis—now supremely successful—will sweep the world.[23]

It would be possible—but scarcely necessary—to multiply the examples. Suffice it to add a few notes on some related formations of ideas.

Psychiatric patients often complain that their minds are being read, chiefly by their psychiatrists. Concepts of how this is done differ, but it usually means telepathy, though without stressing the "tele"—distance is not especially involved. In fact, the mind reading is usually conceived of as occurring in a face-to-face contact, though naturally by way of what, with a now fashionable term, might be called extrasensory perception. Parallels in literature are of course abundant, but they are somewhat outside of the scope of this paper, since they are more characteristic of the older type of tales of the supernatural.

Modern science fiction has a predilection for the trappings of science—if not necessarily for its essence—and generally prefers its mind reading to be done by machine. References to telepathy are nevertheless not rare. "Mutants," especially, and robots are fairly generally described as endowed with telepathic powers.

In the case of the robots, this is the substitute for a power which they do not have —speech. Though in many respects they function on a much higher level of efficacy than humans, they are as a rule dumb. This indicates a feeling for language as something specifically human which would be out of place if attributed to a race of artifacts. The more specific reasons and the possible connection with mutism as a psychotic symptom may be obscure, but it is noteworthy that the same idea was embodied in much older tales, which were well developed long before anybody ever thought of robots. The broom man called into life by the sorcerer's apprentice was dumb; so was the golem of Jewish legend—the clot of clay formed in the shape of a man and animated by having the name of God spoken over it.[24]

When the concept of reading and influencing the mind is elaborated into the idea of effacing and revamping the mental contents of the brain, we come quite close to the fantasy of creating and destroying life (or a semblance thereof)—the core of the stories of the golem and the robot. It is not rare in science fiction to find the motif pushed to its logical extreme: the disintegration and reintegration not merely of organs and their functions, but of entire individuals. The convenient method of splitting a living person into his constituent atoms, relaying them to a distant heavenly body and reconstituting the person there, serves as a means of interstellar transportation in lieu of the spaceship, which to more advanced science fiction writers may appear a bit old-fashioned.

An extreme of somewhat different sort was reached by Ray Bradbury, one of the more renowned among today's science fiction authors. He describes[25] how 16 men in a space ship, taking off from somewhere in Ohio in the year 2000, land on Mars and are understandably nonplussed to find themselves in a small town which is an exact replica of an American town of circa 1927.

Their amazement is topped by the overpowering discovery that the town is populated by their deceased kin—parents, brothers, sweethearts—who, presumably, by the grace of God, have been removed to Mars to live on after death. There are the happiest family reunions, the crew is quickly dispersed into their parental homes, there are embraces and banquets, and finally the delirious joy of retiring to one's own boyhood bed—but then:

> He had the most ridiculous theory quite suddenly. It gave him a kind of chill. It was really nothing to consider, of course. Highly improbable. Silly. Forget it. Ridiculous.
>
> But, he thought, just *suppose* . . . Just suppose, now, that there were Martians living on Mars and they saw our ship coming . . . wanted to destroy us, as invaders, . . . and they wanted to do it in a very clever way, so that we would be taken off guard. Well, what would be the best weapon that a Martian could use against Earth Men with atomic weapons?
>
> The answer was interesting. Telepathy, hypnosis, memory, and imagination.
>
> Suppose all these houses aren't real at all, this bed not real, but only figments of my own imagination, given substance by telepathy and hypnosis through the Martians, thought Captain Black. Suppose . . . these Martians have made this seem like my old home town, my old house, to lull me out of my suspicions. What better way to fool a man, using his own mother and father as bait?
>
> . . . And suppose those two people in the next room, asleep, are not my mother and father at all. But two Martians, incredibly brilliant, with the ability to keep me under this dreaming hypnosis all the time.
>
> . . . Sometime during the night perhaps, my brother here on this bed will change form, melt, shift, and become another thing, a terrible thing, a Martian. It would be very simple for him just to

turn over in bed and put a knife into my heart. And in all those other houses down the street, a dozen other brothers or fathers suddenly melting away and taking knives and doing things to the unsuspecting, sleeping men of Earth . . .

Captain John Black broke and ran across the room. He screamed. He screamed twice.

He never reached the door.

Loss of identity may be viewed—in science fiction as in life—with fear or with longing (or both). Characters in science fiction may have the power of changing their own identity or of robbing the hero of his—in either case paralleling closely the well-known psychotic symptom of depersonalization. The infantile omnipotence which breaks through the barriers of space and time may culminate in the elimination of the self.

It is to be noted that the development of several related motifs shows the same trend: the older stage is characterized by the simple inanimate object and the life-giving magic act; the newer stage by the enormous complication of the inanimate, and by the scientific or pseudoscientific imitation of life. This is the course of development from the golem and the homunculus to the robot; from the ascensions and assumptions of earlier religious fantasy to the space ship; from telepathy to the electric mind-reading machine; from Hauff's demon who implants hearts of stone to J. S.'s general who implants artificial hearts connected by a steel spring; from the medicine man who exorcizes evil spirits to the "electronic psychiatrist."

What are the factors that determine this trend? If we have here a "rapprochement" between the manifestations of psychoses and those of culture, does that mean that changes in the contents of psychotic imaginings reflect changes in culture, or that the culture has become more schizomorph?

Tausk studied the psychotics' ideas of influencing machines.[9] He stressed that the imagined machine has strong elements of a reflection of the human body and that the tendency to devitalize the organism and to ascribe influencing power to lifeless objects is characteristically schizophrenic.

Hanns Sachs, building on the foundations laid by Tausk, explored the "delay of the machine age."[26] Depending on the balance of the dynamic forces within the individuals who form the culture, the energies of society may be directed into different channels, providing or withholding the means to solve certain economic and social problems. Thus classical antiquity, pervaded by narcissism, was unable to create the machines that it would have needed for survival but that it perceived as uncanny. The middle ages did not need them. The postrenaissance era, faced with somewhat similar urgencies as the Greeks and the Romans but no longer bound by their narcissism, has been able to find the answer by developing into a machine age.

Henry Adams, starting from a different approach and using the method of historical-philosophic analysis,[27] arrived at a similar formulation of the great trend with his concept of "the virgin and the dynamo."

All indications are that the "rapprochement" has been mutual—proceeding from both ends.

The content of delusions has become more similar to science fiction, while in older days it used to be more similar to, let us say, religious concepts. This is to be expected, since for the psychotic—like for anybody else—it is easiest to quarry the raw material from which he builds his fantasies in the pits of the surrounding culture.

Manifestations of that culture itself, on the other hand, have become more similar to manifestations of psychosis, a trend which has been proceeding apace with the growing mechanization of our civilization and is part of both its cause and its result. Science fiction is merely one of those manifestations; but it may, because of its peculiarities and its phenomenal rise during the past few years, be considered one of the more remarkable ones. It is a sensitive barometer of our changing mental climate.

We have shown that the similarity between representative science fiction and representative psychotic fantasies is very close—in some cases tantamount to identity. Yet we must not forget that this demonstrated likeness so far is morphologic. The temptation is very great to equate the morphologic with a structural identity. This is what is commonly done when a statement is made like, "this writer is crazy." Translated into scientific terms, this critical opinion would imply the judgment that because a story is morphologically undistinguishable from the content of a delusion, it can be concluded that its author must be suffering from a psychosis that produces such delusions. Surely that would be rash. The actual relationships are more complicated.

The relation of an author to a story produced by him (or, for that matter, of a reader to a story that he absorbs) is undoubtedly different from the relation of a psychotic to a delusion that he produces. It can be stated as an axiom nevertheless that some structural relation between the author and his story exists; that the morphologic similarity of such a story to certain mental disorders is not coincidental; and that conclusions can be drawn from the content and flavor of the story on the mental condition of its author.

The next step is more hazardous. While we can be reasonably certain that some conclusions can be drawn, we are on less secure ground when we are trying to determine just which conclusion is the right one. In order to do this, we would have to know the strength and disposition of the opposing forces in the fight that goes on in the mind of each individual concerned. For each person's ego deals with instinctual energies in a specific way. Those symptoms, dreams, delusions, or stories are arms and armor in that struggle. Dealing with these phenomena under a general rather than an individual aspect, we can merely proffer a general preliminary hypothesis.

The likeliest assumption—within the framework of this reservation—seems to be that the relationship of a creative writer to his literary productions is in the nature of abreaction (as far as the literary creation is socially more acceptable than the writer's daydreams would be, this may also be thought of as sublimation): by objectifying his fantasies in a work which has existence outside of his mind, the writer is able to rid himself of fantasy material that, if not so handled, might indeed get a more personal hold on him and quite possibly emerge as a symptom. Applied to the type of science fiction of which we have brought examples, this would imply two things: primary process material, which eludes the control of the ego and is therefore liable to break forth in psychotic manifestations, is present in the minds of the writers—and by the same token, in the readers. And abreacting this potentially psychotic material through writing (and reading) those stories deprives it of its virulence.

Seen thus, the emergence of science fiction as a major literary genre implies that material of that sort is free-floating in our culture and needs to be abreacted in this way. It is in this sense that science fiction is a barometer of the state of our culture. It would lead us too far afield to attempt to apply the same method to morphologic similarities between certain peculiarities of science fiction and phenomena of sociologic interest, such as the clash of alien civilizations—a pet topic of current science fiction.

The question is bound to arise what practical conclusions may be drawn from all these considerations. Their application is hardly direct but nevertheless of considerable importance. To direct attention to the kinship of psychotic manifestations and of science fiction may be fruitful from both sides: As far as the individual psychotics are concerned, it is always a humbling but also an uplifting experience to discover the rich common ground on which psychosis as well as mental phenomena which are well within the boundaries of the so-called sane both grow. As far as arts and letters are concerned, it is valuable to see the motivating pathologic forces beyond the guise of an elaboration of science in which some literature so much likes to drape itself. Above all, what we all want and need and we can never have too much of, is understanding: understanding of the individual persons with whom we deal as well as of the uncertain directions in which our civilization is moving, sweeping all of us along in its turgid stream.

SUMMARY

The purpose of this paper is to contribute to better understanding of certain aspects of psychotic ideation as well as of some phenomena of our present culture that are not considered to be pathologic. To this end, typical examples of science fiction are subjected to a morphologic and thematic analysis. The concept of morphologic similarity between a literary and a psychopathologic production is introduced. The hypothesis is advanced that science fiction is, to a higher degree than other literature, morphologically similar to schizophrenic manifestations, especially of the paranoid type. Three leading motifs—space travel, survival after a catastrophe, and influencing machines—are reviewed. Pertinent examples from science fiction are confronted with case material taken from the author's own recent observations as well as from existing literature in the field of abnormal psychology. Connections are made with related motifs in legend and folklore and with the question of the evaluation of literary production from the aspect of abreaction. Theories about historical changes in the orientation of civilization are adduced. The relationship between psychosis and science fiction can thereby be seen in perspective. The manifestations with which this paper deals appear as symptoms of growing discomfort in a growingly technical civilization.

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BIOLOGICAL ASPECTS OF AGING

TEN REPORTS OF PAPERS ON GERIATRICS

Hemopoietic Factors with Reference to Aging

Presented by FRANK H. BETHELL, M.D. (University of Michigan, Ann Arbor, Mich.) before the Symposium on Problems of Gerontology, 9th annual meeting of the National Vitamin Foundation and the Johns Hopkins University School of Hygiene and Public Health, New York City, March 2, 1954.

The hemopoietic factors with reference to aging are considered in this primarily clinical paper. Some of the factors involved in influencing hemopoiesis are discussed, i.e. iron, copper, the essential amino acids, the folic acid complex, vitamin B_{12}, other vitamins such as ascorbic acid, the intrinsic factor, and internal secretions such as the hormones.

It is evident then that any aspect of nutrition or physiology that is altered with reference to any of the hemopoietic factors will have an influence in blood regeneration and maintenance of a normal blood picture. Hemoglobin and red blood cell counts tend to decline in advancing years, but this decline is not very great. However, it is greater in the male than in the female. In the female, a tendency for increased values after the menopause is apparent. Although there is no particular decrease in "cellularity" of bone marrow with advancing age, this does not necessarily mean that completely adequate blood factor synthesis is possible under all circumstances in the aged. In individuals over 60 years of age, patients with adequately treated pernicious anemia actually had higher red blood cell and hemoglobin values than so-called normal patients in this same age group. The author also cites evidence and data to support the idea that pernicious anemia is a disease that increases in incidence with advanced age, as is also true of other anemias associated with debilitating diseases. Actually, there are few experimental data that elaborate the factors related to aging that may contribute to anemia. Important among these, however, are cumulative dietary deficiency, hypochlorhydria and achlorhydria, diminution of intrinsic factor, intestinal dysfunction and impaired internal utilization. Gastric hydrochloric acid enhances the absorption of iron, which may play a role in preventing anemias due to impaired iron absorption in aged individuals. It is interesting that both sexes show a general tendency

toward reduced iron absorption with advancing age. There is also an interesting relationship between the incidence of achlorhydria in relatives of patients with pernicious anemia and in patients who are not related to people with pernicious anemia. In the age group under 40, there is an incidence of achlorhydria in some 15 per cent of relatives of pernicious anemia patients, whereas in the age group over 40 this percentage increases to 42 per cent. This is, of course, significantly higher than in groups of subjects not related to patients with pernicious anemia. The intrinsic factor activity of the gastric secretion tends to decrease with advancing years.

The Role of Comparative Physiology in the Study of Aging

Presented by ALBERT I. LANSING, M.D. (Washington University, St. Louis, Mo.) before the Symposium on Problems of Gerontology, 9th annual meeting of the National Vitamin Foundation and the Johns Hopkins University School of Hygiene and Public Health, New York City, March 2, 1954.

The author observes that there are three principal phases in the span of life: infancy, adolescence, and senescence, with, of course, various degrees of infancy and adolescence. Data from three different lines of investigation are presented to support the view that growth and aging are incompatible and that cessation of growth initiates the aging process. Sonneborn's studies of the flatworm, the author's own studies with rotifers, and McCay's nutritional work on rats are cited.

The rotifer provides interesting experimental material for the study of aging because of the many generations that can occur in a relatively short period of time. Furthermore, studies can be carried out under standardized environmental conditions. In this study, life spans of progeny from lines of adolescent, middle-aged, and senile lines of rotifers were investigated. The mean life spans in the adolescent line slowly but significantly increase over seven generations, while middle-aged and senile lines decline and die out over five and three generations, respectively. The mean life span of offspring of adult or senile mothers is reduced. Second generation offspring of adult or senile mothers are reduced. Second generation offspring of older mothers have still shorter life spans, and so on until extinction of the line. The number of generations required to reach such an extinction depends upon the age of the ancestry involved.

The author concludes from his studies that something is transmitted through the eggs of adult or old mothers which actually accelerates aging in the offspring. This effect is not only transmissible but cumulative. Since longevity of offspring of growing mothers is increased rather than decreased, it follows that the aging factor either is not operative or is lacking in eggs of adolescent females. It was also evident that growing rotifers do not contain the aging factor and that middle aged and old rotifers do contain it. Apparently the greater the maternal age, the more marked was the suppression of longevity in the offspring and hence the fewer the number of generations required to produce extinction of the line.

Also discussed is the well-known work of McCay on rats, in which he studied the effect of caloric intake on longevity and showed that animals retarded in their growth by restriction of caloric intake greatly outlived control rats, and further, that these restricted rats were able to resume active growth even after 1,000 days of age. This again emphasized the idea that prevention of maturation almost completely inhibits the process of senescence. From the studies, there appears to be a well-defined antithesis between aging and growth. It is expressed in individual cell lives; intermitotic cells; those that grow and multiply, do not age. It is the postmitotic, nongrowing cells that age. All of these observations emphasize the proposal of the general rule that aging begins when growth stops.

Endocrine Stress and Aging

Presented by DWIGHT J. INGLE, PH.D. (The Ben May Laboratory for Cancer Research, The University of Chicago) before the Symposium on Problems of Gerontology, 9th annual meeting of the National Vitamin Foundation and the Johns Hopkins University School of Hygiene and Public Health, March 2, 1954, New York City.

Some of the endocrine aspects are considered in this paper, with particular emphasis on stress in aging. The author indicates that no single hormone or combination of hormones will reverse the signs of senility. He reviews the role of nonspecific stressors in the physiology of the organism and, particularly, Selye's concept of the adaptation syndrome, which emphasizes the idea that the symptoms induced by stress are similar, regardless of the stressor agent.

The first response to stress reaction is the so-called alarm reaction, resulting in stimulation of the pituitary-adrenal axis, increased production of cortical hormone, and, at this point, an inhibition of growth of the organism. Following this alarm reaction comes the adaptation stage in which many of the signs of stress disappear despite the continuation of exposure to the stressor agent. However, if the stressor agent is present long enough, the stage of exhaustion sets in, in which adaptation fails and signs of stress reappear and may lead to death. Although the alarm reaction and adaptation stage seem to be reasonably well supported by experimental data, the so-called exhaustion stage or exhaustion of adaptation energy is not so firmly established, and more work is needed in this particular area.

In discussing the etiology of the adaptation diseases as a general phenomenon in medicine, the author indicates that this concept grew out of the results of Selye's experiments in which he gave deoxycorticosterone to rats in which one kidney had been removed and who were given a 1 per cent sodium chloride solution as their sole source of fluids. In such animals, severe pathologic changes were noted, hypertension occurred in a large number of animals, and severe renal and myocardial damage was seen. An essential feature of this type of disease production was hormone overdosage of so-called sensitized animals. Although this syndrome has been confirmed in other laboratories, the joint lesion, or arthritic

lesions as reported by Selye, have not been reproduced elsewhere. It is also clear that arteriosclerotic lesions and hypertension occur in these animals.

The question arises whether one can produce these changes under somewhat more natural conditions. It is possible to produce renal damage and hypertension in sensitized rats that are exposed to cold. However, such animals double their food intake, and the results of damage seen may not be necessarily related to endocrine function per se but may actually be due to the increased load of metabolizing the increased food and sodium chloride ingested by these animals. Of great interest is the report that serious damage was found in aging female rats that were discarded breeders—animals that had not been exposed to unusual stress conditions other than that of raising several litters of young. The kidneys, heart, and aorta of these animals were very severely damaged, indicating clearly that spontaneous degenerative changes can and probably do occur much oftener than is suspected in experimental work with animals over long periods of time. This of course opens up an exciting area of research, trying to reproduce these findings and studying the various factors that may be involved in the production of the lesions seen.

The Present Status of Physiological and Biochemical Studies of Aging

Presented by NATHAN W. SHOCK, PH.D., (Baltimore City Hospitals, Baltimore, Md.) before the Symposium on Problems of Gerontology, 9th annual meeting of the National Vitamin Foundation and the Johns Hopkins University School of Hygiene and Public Health, New York City, March 2, 1954.

Aging, or the problems of gerontology, was the featured subject at a symposium sponsored by the National Vitamin Foundation held at the Biltmore Hotel in New York on March 2, 1954. Perhaps the over-all importance of this symposium can be best summarized by the fact that it emphasized how little we know about the problem of aging and the factors that influence old age. This symposium did, however, serve to bring into sharp focus the many aspects of the problems of aging and approached the problem of aging from various points of view. Following is a summary of the papers that were presented at the symposium in chronologic order.

This paper on some of the physiologic and biochemical aspects of aging defines aging as changes that take place in an organism with time, particularly those changes that are seen after cessation of growth. One of the important problems of aging is why a cell loses its ability to maintain its integrity. What, for example, are the differences that exist between young and old animals? The emphasis is placed on the functional changes that occur with time, outside the realm of degenerative diseases and other disease states that appear in the aged. The question was also raised whether aging is a pathologic process or a biologic phenomenon proceeding in the absence of all other known or diagnosable disease. In attempts

to answer some of these questions, experiments are reported which showed that little differences in the absorption of vitamin A was apparent in elderly patients after giving them a 100,000 unit dosage of vitamin A, and that there was no significant difference noted in the elevation of plasma vitamin A and carotene levels between the aged and young individuals. Interesting studies on changes in renal function in old age compared with those in young individuals are reported. The Diodrast clearance, or the estimate of renal plasma flow, falls significantly in the aged compared with the young, although there are widespread individual differences between subjects. These careful studies, however, indicated that in the aged there is a reduced number of active kidney nephrons and a general diminution of function. It was also noted that water diuresis was shut off more effectively in young than in aged patients on administration of anti-diuretic hormone. This was taken to represent evidence for a change in cellular metabolism in the aged individuals.

Changes in basal metabolism in the aged were also considered in a report. The classic information on this subject indicates a general downward trend of the basal metabolism with advancing age. These data are based on the surface area law and, since some criticism can be leveled against this concept, a re-evaluation was made, based on the metabolism in reference to the water content of the body. When the oxygen consumption was evaluated on the basis of the body water content, there was no indication of changes in oxygen consumption in the aged.

Fat Metabolism with Particular Reference to Problems of Aging

Presented by H. J. DEUEL, JR., PH.D., (University of Southern California, Los Angeles, Calif.) before the Symposium on Problems of Gerontology, 9th annual meeting of the National Vitamin Foundation and the Johns Hopkins University School of Hygiene and Public Health, New York City, March 2, 1954.

Studies on fat metabolism and aging are rather limited in number, but the author cites data from some very provocative experiments and emphasizes certain changes in relation to sex changes in the female that affect the problem of aging. Changes in the distribution of fat and water content of the body are notable in advancing age. A gradual increase in the fat deposits of the body occurs as age advances. Water content of the body, on the other hand, varies inversely in proportion to the fat content, decreasing as age increases.

Blood lipid changes are less definite in their pattern of change. The work of Keys shows a progressive increase in blood cholesterol with advancing age. There does not appear to be a similar consistent change in the pattern of some of the other blood lipids, particularly the phospholipids. A difference in the chylomicron content of blood in the aged can also be seen; in general the chylomicron count is elevated in older age, presumably because of a decreased ability to emulsify fat,

and is thought to be related to decreased pancreatic function in the aged. Of interest were the studies reported on changes with age in the essential fatty acid content of livers of rats. The author thinks there is reasonable good evidence that the requirement for essential fatty acid may increase in old age, based on studies with the rat. However, no definite conclusions can be drawn from this work with regard to man.

Some Observations on Blood and Urine Vitamin Levels in the Aged

Presented by JOHN ESBEN KIRK, M.D. (Washington University, St. Louis, Mo.) before the Symposium on Problems of Gerontology, 9th annual meeting of the National Vitamin Foundation and the Johns Hopkins University School of Hygiene and Public Health, New York City, March 2, 1954.

Observations on the blood and urine vitamin levels in the aged are reported from two basic types of surveys, i.e. general population surveys conducted by various workers, and institutional nutritional surveys, in which patients under controlled conditions in institutions were studied for the vitamin levels of their blood.

In the population survey studies, there appeared to be little difference in carotene or vitamin A level in serum between young and old subjects. There is a tendency, however, toward a lower than normal vitamin A value in several old and young individuals. There is some evidence that ascorbic acid may show a decline in concentration in blood with advancing age, particularly in population groups whose diets contain a suboptimal amount of vitamin C. On the other hand, riboflavin serum values are not changed significantly with advancing age. This appears also to be true for the pantothenic acid excretion in the urine.

Also reported are studies on the vitamin A serum content, vitamin B_1 blood level, and the DPN concentration of the red blood cells in institutionalized patients receiving approximately 2,100 calories per day. The mean levels of these vitamins under these conditions were in the normal range. The institutional studies showed that ascorbic acid was apparently the only vitamin that significantly decreased in the blood with advancing age. Several of the old subjects, however, had subnormal blood concentrations of vitamin B_1. It was found that if vitamin B_1 is given in tablet form in a dose of 5 mg. daily, enough thiamine is supplied to insure normal blood values of B_1 for the subject. But, even with such supplementation of thiamine, as much as two-thirds of the administered dose may appear in the feces. The author emphasizes that in an attempt to evaluate vitamin nutrition with respect to the utilization of administered doses in old individuals, it is important to consider each vitamin separately, since there seem to be variations with regard to the absorption of the vitamins and their destruction in the gastrointestinal tract. Of the various factors involved in possible losses of vitamins in aged individuals, it appears that modifications with age in the intestinal flora may be of particular importance.

Protein Metabolism—with Particular Reference to Problems of Aging

Presented by CHARLES S. DAVIDSON, M.D. (Thorndike Memorial Laboratory, Boston, Mass.) before the Symposium on Problems of Gerontology, 9th annual meeting of the National Vitamin Foundation and the Johns Hopkins University School of Hygiene and Public Health, New York City, March 2, 1954.

Clinical problems of aging are particularly emphasized. A picture of an elderly individual in which there was severe evidence of malnutrition and tissue wastage is described as a frequent sight in many typical hospital wards. This typical case is evidence of the undesirable attitudes of many aged people toward obtaining adequate and proper nutrition. Evidence is cited that there is loss of protein with aging. First there appears to be an increase in the percentage of underweight people in advanced age groups, characterized by a decrease in lean body mass and protein content. Also important to consider is the fact that obesity may frequently hide or confuse the issue in terms of the decreased body protein mass. Some of the factors that influence this decreased body protein mass in aged individuals were emphasized, such as the frequently decreased intakes of foodstuffs and of protein. This raises the question whether or not the requirement for protein is altered in the aged. Data of this type are rather limited, but the author doubts that there is very little alteration in the protein requirements in the aged. Some of the more pertinent reasons for reduced food intake and for reduced protein intake were outlined, such as the changed attitude of aged individuals toward getting good food. In other words, they lose interest in eating, spend very little time in meal preparation, and are quite content with the usual crackers and tea, or bread and jam, or some other easily prepared foodstuff that contributes little in the way of protein but generally a great deal in the way of carbohydrate. The author speculates on the possibility that decrease in lean body mass in males may be due to a decrease in the production of testosterone, but little work has been done in this area. There is little or no evidence of a relationship between decrease in ovarian function and decrease in muscle mass. Frequently in the aged there appears to be some clinical evidence of a relationship of adrenal insufficiency to old age. On the other hand, adrenocortical function does not seem to be impaired in the aged, as reflected by ACTH stimulation—it is the general appearance of the aged individual that is remindful of Addison's disease, rather than actual impaired functioning of the adrenal cortex as established by studies on adrenal stimulation. Very few studies have been made on the pituitary function in old age, but in man there appears to be a decrease in the size and weight of the pituitary. There is actually little solid information about the role and function of the endocrines in aged individuals. Nutrition plays a very important role in many of the diseases of old age and may contribute to the problem of aging.

Special Nutritional Problems of the Aged

Presented by HENRY A. RAFSKY, M.D. (Geriatric Institute, Home and Hospital of the Daughters of Jacob, New York) before the Symposium on Problems of Gerontology, 9th annual meeting of the National Vitamin Foundation and the Johns Hopkins University School of Hygiene and Public Health, New York City, March 2, 1954.

Some of the special nutritional problems of the aged are discussed in this paper. The author says that, although he has seen few real clinical signs of avitaminosis in his work, the biochemical lesions as indicated by serum levels of some of the vitamins indicated partial deficiency. This was illustrated by low serum carotene and vitamin A values in a significant number of these elderly subjects. Observations also showed that elderly people seem to be "partial to carbohydrate." This may be partly a reflection of their inability to masticate and handle the more solid protein foods such as meat, and also the fact that many of the carbohydrate foods are much simpler to prepare and to consume.

The incidence of protein deficiency is seen often in aged subjects. Although studies revealed that the total protein content was within the normal range of 6 to 8 Gm. per 100 cc. of plasma, the author found a significant decrease in albumin and increase in the globulin fraction of the plasma protein. This was particularly evident in an increase in the beta globulin fraction. This type of observation is of interest in reference to the possible alterations in lipid-bearing proteins in blood of older individuals. Increased hepatic dysfunction was evidenced in as many as 80 to 90 per cent of aged individuals. In studies of vitamin A, impaired utilization, rather than impaired or reduced absorption, was found. The use of crude liver extract seemed to improve significantly the symptoms of fatigue in many of these elderly individuals. This crude liver seemed to be more effective than the B complex vitamins alone. The absorption of vitamin B_{12} by aged individuals was much lower than that of young individuals. Data indicated that the tissue saturation of vitamin B_{12} in the aged was not as great as in young individuals.

The Absorption of Vitamins and Enzymic Activities in Aging

Presented by BACON F. CHOW, PH.D. (The Johns Hopkins University, Baltimore, Md.) before the Symposium on Problems of Gerontology, 9th annual meeting of the National Vitamin Foundation and the Johns Hopkins University School of Hygiene and Public Health, New York City, March 2, 1954.

The use of an oral tolerance test for determining the absorption and utilization of B_{12} in human subjects is described. This test consists of first obtaining a fasting blood sample, then feeding a large dose of vitamin B_{12}, followed by the withdrawal of two additional blood samples at 1½ and 3 hours later. All of the blood samples

are then analyzed for their vitamin B_{12} content. The normal level of vitamin B_{12} in young individuals was approximately 250 micromicrograms, and there was a 90 per cent response to a 1 mg. dose of oral vitamin B_{12} in 10 out of 11 young subjects.

In a similar study carried out with old people (averaging 70 years of age) there was only a 40 per cent average response in 14 out of 36 subjects after a 1 mg. dose of oral vitamin B_{12}. Old people have a lowered vitamin B_{12} binding capacity, generally reflected by their increased tendency toward achlorhydria; perhaps they have a lowered content of intrinsic factor available for binding vitamin B_{12}. Further evidence that old people may not be as adequately nourished with respect to vitamin B_{12} as young patients is the fact that when vitamin B_{12} is injected in old individuals, more of it is retained than in the young. This is interpreted to mean that there is less tissue saturation in old subjects, hence they retain more of the vitamin when it is injected. Because of the ever-increasing rôle of vitamin B_{12} in metabolic processes, the implications of these studies are very important.

The Hormones and Metabolism

Presented by C. N. H. LONG, M.D. (Yale University, New Haven, Conn.) before the Symposium on Problems of Gerontology, 9th annual meeting of the National Vitamin Foundation and the Johns Hopkins University School of Hygiene and Public Health, New York City, March 2, 1954.

In studying the general principles underlying the role of hormones that influence metabolism, the important interrelationships of carbohydrate, protein, and fat metabolism are stressed. Shifts can occur in the metabolic substrates under influence of hormones, but it is important to note that if a shift to increased carbohydrate metabolism is seen, then shifts in protein and fat metabolism are also occurring. For example, the so-called ketogenic hormone, once reported to be involved in increased ketone body production, could easily be a reflection of decreased carbohydrate utilization and metabolic factors involved with this decrease in carbohydrate consumption by the individual, which necessitated an increase in fat metabolism. The author further pursues the idea that aging begins where growth ends by redefining it in terms of anabolism and catabolism in the total metabolism of foodstuffs and body tissue. One might visualize the aging process as beginning when the anabolic processes tend to give way to those of catabolism. The work carried out in the production of pancreatic diabetes with such substances as ACTH, the adrenalcorticoids, and the pituitary growth hormone is reviewed. The role of cortical hormones in producing glucose from protein via the mechanism of gluconeogenesis is pointed out as a catabolic activity directed against protein synthesis, in general evidence of a drain against the protein stores of the body. However, the cortical hormone influencing carbohydrate metabolism provides a mechanism whereby the body can be supplied with glucose under stress conditions, such as that of fasting. This role of carbohydrate metabolism is further em-

phasized by the fact that if the cortical hormone (cortisone) is given to fed mice, one sees great increases in the storage of liver and muscle glycogen.

Continued large doses of the hormone, however, lead to glycosuria and a marked decrease in sensitivity to insulin. This is clear example of the production of a "steroid diabetes." Emphasis is placed on increasing incidence of diabetes mellitus in this country, particularly on the whole role of obesity in relation to this increased incidence. Diabetes mellitus and obesity are diseases of the overnourished, and a great deal more work needs to be done to elucidate factors involved in overnutrition and obesity. That obesity is a problem in diabetes is clearly indicated by the fact that if the body weight of many of these obese individuals is reduced, the diabetes can often be curbed significantly. This of course, unfortunately, does not apply to all individuals. The reason why overeating and the subsequent increase in fat deposition lead to such an increased incidence of diabetes is discussed, and reference is made to the Yale laboratories' experimental production of obesity as the result of producing a lesion in the hypothalamus in rats. Such a "hypothalamic-damaged" animal gains a tremendous amount of weight (increase in body fat) and his food intake is very great. A reduced carbohydrate tolerance and occasionally frank diabetes is the consequence of such overeating and excessive obesity in such animals. This increase in the incidence of diabetes emphasized the fact that insulin is concerned in the transformation of carbohydrate to fat. In individuals who ingest a caloric excess continually, these calories are laid down as fat, and this extra fat synthesis requires additional units of insulin, an increased strain on the pancreas; in a significant percentage of individuals, it can lead to diabetes. Very little is known concerning the effects from an increased caloric intake.

Reports of Papers From Other Meetings

Changes in the Brain Following Smallpox Vaccination

Presented by VERA B. DOLGOPOL, M.D.; MORRIS GREENBERG, M.D.; AND ROSA ARONOFF, M.D. (Willard Parker Hospital, New York; Department of Health of New York; and Greenpoint Hospital, Brooklyn, respectively) before the annual meeting, American Association of Pathologists and Bacteriologists, Philadelphia, April 8–10, 1954.

Three patients with postvaccinal encephalitis, characterized by perivascular softening of myelin, adventitial neutrophilia, and hyaline thrombi, were reported by the authors.

The first was a 5½ month old infant who died of pertussis. The infant had been vaccinated seven weeks before death. The spinal fluid was found normal. Microscopic examination revealed adventitial infiltration of lymphocytes and phagocytes; the extra-adventitial tissue was infiltrated with glial cells. This picture was similar to that described previously for the subacute stage of postvaccinal encephalitis.

The second patient had vaccinia. Here skin became denuded and the extrem-

ities spastic shortly before death, which occurred 9 days after the skin lesions appeared. The brain showed a great many veins with walls infiltrated by large mononuclear cells. Granular and hyaline material was also seen. There was a minimal breakdown of myelin around the several veins. The demyelinization was slight, probably because the patient died less than one day after neurologic symptoms had begun, and the demyelinating lesions had no chance to reach full development. Two other vaccinated patients died, but lesions of the brain were not those of postvaccination encephalitis.

One of those patients was operated on, under spinal anesthesia, one day after vaccination. On the fifth postoperative day the patient was doing well and was up and about. On the sixth day she developed fever and neurologic signs, and she died five days later. Myelin degeneration was present but unrelated to vessels. The Betz cells were ballooned by lipoid material (this does not occur in postvaccination encephalitis). The pia and arachnoid were thickened.

The other patient had slight lymphocytic infiltration of the vascular walls in the brain and lumbar cord. There was no degeneration of myelin. The patient died five days after the onset of neurologic symptoms.

Diet and Arteriosclerosis

Presented by MICHAEL G. WOHL, M.D. (Temple University, Philadelphia, Pa.) before the 18th annual Postgraduate Institute and Convention, Philadelphia County Medical Society, Philadelphia, March 30–April 2, 1954.

There is no conclusive evidence that atherosclerosis in man can be prevented or effectively treated by withholding cholesterol from the diet. Atherosclerosis is due neither to hypercholesterolemia nor to a deficiency of lipotropic substances.

Arteriosclerosis is a generic term applied to a group of vascular diseases, of which atherosclerosis is one. The pathology of atherosclerosis will be reviewed. Cholesterol synthesis, absorption, and destruction will be outlined.

Arteriosclerosis is a leading cause of death. It may be related to disturbances of lipid metabolism. Primary factors in atherogenesis are lipid infiltration of intima and changes in the blood vessel walls. Whether these are primary and lipid deposition secondary is not definitely established.

There is good evidence of a relationship between atherosclerosis and cholesterol: (1) Atheromas are composed mostly (50 to 60 per cent) of cholesterol and its esters. (2) Certain hypercholesterolemic conditions, such as xanthomatosis, myxedema, nephrosis, and diabetes mellitus, are accompanied by atherosclerosis. (3) Persons with coronary artery disease tend to have elevated blood cholesterol values; however, coronary thrombosis is a poor indicator of atherosclerosis in the vascular system as a whole. High cholesterol diets produce atherosclerosis in animals. Whether this holds true for man is dubious, however, since many times as much

cholesterol as is contained in a normal diet must be fed, and it produces a hypercholesterolemia in animals only, not in humans.

The body is capable of synthesizing cholesterol from *any food*. The liver is the main organ of synthesis, and 1.5 to 2 Gm. daily are synthesized, much more than is ingested in the diet. The blood cholesterol level is not affected by the diet.

The evidence implicating disordered lipid metabolism in the pathogenesis of atherosclerosis is discussed. Factors other than abnormal sterol metabolism in atherogenesis are considered. These factors are: mechanical; hereditary; endocrine; anatomic changes of vessel wall, and physiologic state of blood lipids.

The author then reviews the practical application of interrelated factors concerned in human atherosclerosis. He stresses the fact that previous observations point to the correlation between overnutrition and atherosclerosis. The practical measures for controlling atherogenesis, therefore, are avoidance of excessive caloric intake and control of obesity by subcaloric diet.

Restriction of dietary cholesterol, however, has little effect on blood cholesterol levels. Extremely low fat diets may reduce hypercholesterolemia by retarding cholesterol absorption from the intestines. Extremely low lipid diets are not recommended for long-term application, since they are impractical and, if prescribed, must be supervised by both dietitian and physician. Samples of low fat diets are presented.

Present Status of "Curare" Drugs

Presented by ROBERT D. DRIPPS, M.D. (Hospital of the University of Pennsylvania) before the Philadelphia County Medical Society Scientific Meeting, Philadelphia, March 10, 1954.

One hundred million doses of curare drugs have been sold in the past decade and their use is becoming even more common. They are used to minimize the deeper planes of general anesthesia: to "reduce hangover." In medicine they are used in spasticity, rigidity, and in the spasm and pain after fracture and strains.

There are several hazards in the use of these drugs. There may be respiratory depression, often with cessation of breathing, and this can persist for hours. This is rare, however, and can be predicted with test doses. The drugs are ganglionic blocking agents, and may produce hypotension and intolerance to changes in position. They also may block central nervous system conduction. This phenomenon may be the reason why respiration can be blocked with other movement possible. Other hazards in their use are due to ancillary agents, such as the adjunctive use of Pentothal.

Dermatological Disorders Commonly Encountered in General Practice

Presented by MARION B. SULZBERGER, M.D., (Dept. of Dermatology and Syphilology, New York University Post-Graduate Medical School; Skin and Cancer Unit, University Hospital, New York) before the Annual Conference, Chicago Medical Society, Chicago, Ill., March 2–5, 1954.

Dr. Sulzberger stated that ten groups of diseases are estimated to make up about 90 per cent of the conditions dermatologists are called on to treat. Fifteen per cent of all patients coming to physicians have complaints related to dermatology or syphilology. In the Air Force, skin diseases are the third highest cause of hospitalization and of sick days.

Acne Vulgaris: 80 to 90 per cent of adolescents have this condition to some degree. It occurs at the very worst psychologic time—adolescence; and since it affects character and the future of the patient, treatment is important.

Androgen (or perhaps progesterone in females) is the exciting stimulus and the hair follicles and the sebaceous glands of the face, neck and back are the target areas.

TREATMENT

(1) The first step is to prevent the glands from being plugged and to bring about the removal of plugs which may have formed. This can be done by washing regularly and vigorously with soap and hot water, using a cloth or a complexion brush. The desirable slight peeling and drying of the skin can also be accomplished with 2 to 5 per cent resorcin combined with 3 to 10 per cent precipitated sulfur in a lotion, cream, or ointment. Peeling with dry ice in slush form or ultraviolet light may also help in some cases.

(2) Another phase of treatment is reduction of the activity of the sebaceous glands, which can be done by roentgen rays. The doses needed for this beneficial effect are not harmful when properly given by qualified skin specialists.

(3) In another approach the circulating androgens can be counteracted by the administration of female sex hormones. When there is no disease of the female genitalia or breasts, 0.625 mg. to 2.5 mg. of premarin daily, by mouth for 10 to 12 days before the menstrual period, may prove useful in females.

(4) A fourth phase of treatment is the prevention of accumulation of secreted and excreted substances in the orifices of the plugged glands. When these substances are derived from infectious microorganisms, either locally in the follicles or living at a distance, improvement may be achieved by wide spectrum antibiotics in small doses given orally over long periods (together with the necessary adjuvants of vitamin B complex and repeated checks of the blood picture, etc.). When common foods are the causes of attacks, these must be avoided. Among the most common offenders are chocolate, pork, and shellfish, but in occasional cases almost any food can be to blame. The accumulation of irritating drugs in the follicles, (such as bromides and iodides) must be prevented by eliminating the

offending exposures. Mechanical irritation, trauma, friction from rough clothing, maceration, the wearing of woolens, etc., exposure to pitches, tars, and waxes, etc., can cause follicular closure and follicular irritation and should be avoided. The goal of acne treatment should be to keep the skin feeling slightly tight and dry but not so dry as to cause scaling, severe discomfort, and disfigurement.

THE MANAGEMENT OF ATOPIC DERMATITIS WITH REMARKS ON ACTH, CORTISONE AND HYDROCORTISONE

It is clear that ACTH and cortisone are often lifesaving measures and should be used whenever indicated in pemphigus, acute disseminated lupus erythematosus and some other ordinarily fatal skin diseases. The ACTH and/or cortisone will often bring the disease to a standstill but does not cure it, unless nature cures the disease with time.

In cases of pemphigus, huge doses of these hormones are sometimes given—as high as 1,000 mg. of oral cortisone per day in the beginning and then a gradual reduction of dose stepwise and very slowly over several months to years. Some patients who were initially on such high doses two to three years ago are now in satisfactory remissions and living normal, useful, and happy lives on small doses (e. g., 20 mg. to 50 mg. daily) or even without any hormone treatment at all at present.

In severe, otherwise intractable, atopic dermatitis, about 75 mg. to 200 mg. of oral cortisone per day are given at the beginning. This dose can often be reduced very gradually over several months to reach the smallest "morbistatic" dose, i.e., the smallest dose which will still maintain the patient in a reasonable degree of comfort and as a useful human being. Sometimes doses in the order of from 25 mg. to 5 mg. per day are required over long periods of time but there are other cases in which the dose can be reduced to zero as the disease become stabilized and the patient improves.

Because of the constant undeniable risks of severe effects from the systemic administration of ACTH and/or cortisone, the *hydrocortisone* preparations which can be applied *locally* were a great advance and a welcome addition. These preparations have none of the risks of the systemic effects and no demonstrable effects of absorption, even though applied by inunction over one third of the body surface daily. They are, in Dr. Sulzberger's opinion, one of the most effective external therapeutic agents ever studied by his group. While their value is almost negligible in psoriasis, pemphigus, and lupus erythematosus, they are decidedly beneficial in about 75 per cent of the cases of atopic dermatitis (including infantile eczema), anogenital itching, eczemas of the eyelids, hands and elsewhere, otitis externa, and many other common dermatoses. However, the full usefulness of this form of medication is today restricted not only because it is "morbistatic" and must be used over long periods of time in chronic diseases, but also because it is at present still so expensive for long-term use on extensive areas of skin involvement. The cost is within reason in self-limited dermatoses on small areas; and one may look forward to progressive reductions in price as the demand for the

material increases and the manufacturing processes improve. The local effectiveness of hydrocortisone treatment is teaching physicians many things—not the least of which is that contrary to some prevalent beliefs. Many itching and disfiguring dermatoses affect the emotions more than the emotions caused the dermatoses ("somato-psychic" effects as contrasted with "psychosomatic" effects).

Evaluation of the Newer Drugs in the Treatment of Hypertension

Presented by C. T. BELLO, M.D., (Temple University Hospital, Philadelphia, Pa.) before the 18th annual Postgraduate Institute and Convention, Philadelphia County Medical Society, Philadelphia, March 30–April 2, 1954.

The posterior hypothalamic area, which influences the vasomotor center, may be influenced by *Rauwolfia serpentia* and its active alkaloids. The vasomotor center, which controls vasomotor tone, is affected by apresoline, which diminishes vasoconstriction. Twenty-five to 100 mg. are given orally every four hours. Nausea, vomiting, tachycardia, nasocongestion, and postural hypotension may be encountered. The autonomic ganglia are influenced by the tetraethylammonium ion. Nicotine also acts here. One hundred to 500 mg. of TEA produce a response within seconds. Side reactions include mouth dryness, metallic taste, and postural hypotension. The parasympathetic ganglia may be blocked by the hexamethonium ion. This has a long duration of action. It frequently causes constipation, and even anuria may result. Two hundred and fifty to 500 mg. of the salt are used orally, or 15 to 25 mg. of the ion parenterally. The neuroeffector junction is blocked by dibenamine, 2 to 5 mg. per Kg. I.V. This causes severe postural hypotension, local irritation, phlebitis, tachycardia, tremors, and hallucinations. Dibenzyline has ten times the potency of dibenamine. It is used orally or parenterally. The dose is 0.2 to 0.5 mg. per Kg. I.V. Apresoline also has a sympatholytic effect. Dihydroergocornine is used in a dose of 1 to 2 mg. every four hours. Priscoline is used in peripheral vascular disease—25 to 50 mg. every four hours. Benzodioxane and regitine are used in tests for pheochromocytoma. Veratrum virde and its alkaloids (veriloid and proveratrine A) effect the reflex vascular arcs, which may influence the blood pressure and heart rate.

Isolated Maxillary Sinus Affections

Presented by WALTER P. WORK, M.D., (Stanford Medical School, Dept. of Otorhinolaryngology, San Francisco, California) before the 23rd Annual Spring Clinical Conference, Dallas Southern Clinical Society, Dallas, Texas, March 15–18, 1954.

In acute maxillary sinus infections, the patient should be put to bed, culture

taken (and only the pathogens considered), and antimicrobial drugs started. *No* manipulation should be done during the acute phase.

In chronic maxillary sinus infections conservative therapy is started first. This includes antimicrobial drugs and irrigating the sinus with saline or Ringers solution every four to five days. This Rx is carried out for 18 to 21 days. If conservative therapy fails, surgery will probably have to be done for relief of the sinusitis. The most conservative type of surgery compatible with a cure is advocated, and the more radical sinus surgery, such as the Caldwell-Luc procedure, is reserved for recalcitrant cases. All predisposing factors are also eliminated as part of the routine therapy.

Further Studies of the Etiologic Agent of *Pemphigus Vulgaris*

Presented by ARTHUR W. GRACE, M.D., (State University of New York, College of Medicine, New York City) before the Medical Research Forum, N. Y. Academy of Medicine, New York City, January 28, 1954.

Since 1937 Dr. Grace and his co-workers have been publishing data which tend to indicate that there is a virus type etiologic agent involved in *pemphigus vulgaris*. Additional work presented in this report showed that the serum titer of neutralizing antibody in humans with *p. vulgaris* varied directly with the severity of the disease. With deterioration of the patient with pemphigus, the serum content of neutralizing antibodies decreased, and with improvement in the clinical condition, there was noted a concomitant rise in the titer of neutralizing antibody. At death, in one patient, no neutralizing antibody was found to be present in the blood.

Some Abnormalities in Pyridoxine Metabolism in Human Beings

Presented by RICHARD W. VILTER, M.D. (Department of Internal Medicine, University of Cincinnati) before the Nutrition Institute (Symposium on Basic and Applied Studies of the Newer B-Complex Factors) of the Federation of American Societies for Experimental Biology, Atlantic City, April 12–16, 1954.

The clinical manifestations of vitamin B_6 deficiency, induced in human beings by synthetic diet or an antimetabolite, are as follows: in infants—convulsions and anemia; in adults—seborrheic dermatitis of the sicca type, glossitis, stomatitis, peripheral neuritis, convulsions, and increased susceptibility to infections.

The administration of vitamin B_6 prevents the development of toxic symptoms in the treatment of tuberculosis with the new anti-TB drug, isonicotinic acid hy-

drazide. Evidence has been obtained only recently that vitamin B_6 metabolism may be affected adversely by isonicotinic acid hydrazide (isoniazide or INH), a drug that has been used very effectively in the treatment of tuberculosis. When INH is given in the usual therapeutic dose, only occasionally do toxic manifestations occur in the form of peripheral neuritis. When the dose is increased, 40 per cent of the patients develop neuritis before the fifth to eighth week. When INH is given, vitamin B_6 appears in the urine in very large amounts, usually five to seven times the amount present before INH administration. Xanthurenic acid excretion following tryptophane also increases in an erratic fashion. In general, the higher the dose of INH, the greater these abnormalities are.

Vitamin B_6 deficiency can develop when diets are limited to specially processed foods. Infants fed a commercial liquid milk formula developed convulsions in the third or fourth month of life. The etiology of these convulsions was obscure until investigation showed that the milk had become very deficient in vitamin B_6 during processing. This vitamin relieved the convulsions and the abnormal electroencephalographic pattern accompanying them. The author also thought that a local metabolic defect might exist in the skin of persons with seborrheic dermatitis of the sicca type, which increased the local need for vitamin B_6. Such an increased need for vitamin B_6 could not be met by oral or intramuscular administration of the vitamin. These lesions improved, however, when a 1 per cent pyridoxine or B_6 ointment was applied four or five times a day.

CLINICAL STUDIES ON ANTICANCER AGENTS, 1952-53

(*Continued from page 406*)

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